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THE SURGICAL TREATMENT OF COMPLETE TRANSPOSITION OF THE AORTA AND THE PULMONARY ARTERY

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COMPLETE transposition of the aorta and pulmonary artery is a relatively common congenital anomaly. In complete transposition of the great vessels the aorta arises from the ventricle receiving systemic venous blood and the pulmonary artery arises from the ventricle receiving oxygenated blood. Blood that is pumped by the left ventricle through the pulmonary artery to the lungs returns by the pulmonary veins and left auricle to its point of origin in the left ventricle. Blood that is propelled by the right ventricle through the aorta to the body is returned by the systemic veins and the right auricle to its starting point in the right ventricle. In other words, there is transposition of the great arteries without transposition of the great veins. The systemic and pulmonary circulations are thus basically separate; a condition obviously incompatible with long survival. However, there is generally some degree of communication between the two circulations by way of septal defects or other abnormalities. These abnormal communications allow some oxygenated blood to be shunted into the systemic circulation, and some venous blood is similarly transferred to the pulmonary circulation.

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Because of these compensating abnormalities certain individuals with transposition may survive for a long time. The usual life expectancy, however, is quite short. In 123 collected cases (4) the average duration of life was 19 months. If 6 patients who lived 10 years or longer are excluded, the average duration of life for the remaining 117 patients was only 5½ months.

We have discussed elsewhere (4) the relation between longevity and the presence of specific abnormalities associated with complete transposition. As might be expected, the duration of life depends on the degree of mixing between the two circulations. A ventricular septal defect is associated with the greatest life expectancy in these patients, presumably because it results in the best interchange of blood between the two circulations. Patency of the auricular septum is the next most favorable isolated defect and the combination of an auricular and a ventricular defect gives an even better prognosis. Various other abnormalities may provide a means of mixing between the systemic and pulmonary circulations in cases of transposition. Among these are patent ductus arteriosus, and partial transposition of the great veins.

Surgical therapy for transposition of the great cardiac arteries might reproduce any of the defects previously mentioned. It is tech-

nically feasible to establish an artificial patent ductus arteriosus (1), to transpose a portion of the venous return to the heart (4), and to create an auricular septal defect (2). Experimental investigation of the therapeutic effect of such measures has been hindered by the difficulty of producing complete transposition of the aorta and pulmonary artery in laboratory animals. Despite the preliminary establishment of certain corrective shunts, all of our animals with artificial transposition of the great cardiac arteries have succumbed soon after production of the transposition. Details of these investigations will be discussed elsewhere.

Treatment of patients with transposition of the great vessels is based on measures which have been proved to be surgically feasible even though their therapeutic effects cannot yet be tested in the laboratory. The poor prognosis and severe incapacity of these patients justify the use of any method which offers reasonable hope of improvement.

Taussig (5) clearly described the clinical features of transposition in 1938. In her recent classical monograph (6) on congenital malformations of the heart, the pathognomonic features of this condition are given as: "the narrow aortic shadow in the anterior-posterior position and the wide aortic shadow in the left anterior-oblique position, combined with enlargement of both ventricles and the absence of the fullness of the normal pulmonary conus of the right ventricle." Murmurs are of no diagnostic importance and chief reliance is placed on fluoroscopic examination. There are increased vascular markings in the lung fields and in many cases vigorous pulsations of the pulmonary arteries are visible. The various abnormalities associated with the basic condition of transposition give rise to certain recognizable clinical syndromes, but there are so many varieties of transposition that it is not always possible to make an accurate anatomical diagnosis.

In attempting to clarify these confusing problems, angiocardiography has been carried out by Drs. Robert Cooley and Robert Sloan of the Department of Radiology. This procedure serves to confirm the diagnosis and may furnish information concerning the type of communication between the two sides of the heart. The accompanying reproduction (Fig. 1) of an angiocardiogram on one of the cases discussed hereafter demonstrates well the characteristic anterior origin of the aorta although the nature of the intracardiac shunt is not clearly shown.

Catheterization of the cardiac chambers is of little assistance in diagnosis of transposition, but once the diagnosis has been established, considerable information may be secured concerning the internal hemodynamics of the heart. These considerations have been given in detail by Bing and his associates (3).

SURGICAL TREATMENT

Some operative procedure has been attempted on 33 patients who were believed to have transposition of the great vessels. The ages of the patients ranged from 8 days to 8 years. Fourteen of the patients were less than 10 months of age. In each instance the diagnosis was made by Dr. Helen Taussig and her associates and corroborated by operation or autopsy or both. Miss Olive Berger anesthetized all of these patients. It is a tribute to her skill that only 4 of these extremely ill children died during the operation and that none of the deaths appeared to be due to anesthesia.

The operations fall into three main groups:

I. Construction of extracardiac shunts, either venous or arterial.

II. Creation of an auricular septal defect.

III. Creation of an auricular septal defect plus an extracardiac arterial shunt.

I. Construction of extracardiac shunt, either venous or arterial. In this category are included 9 of the first 10 operations. They comprise arterial, venous, or arteriovenous shunts between systemic and pulmonary vessels. All of these operations are designed for the same purpose, namely, to direct some blood back to the side of the heart opposite its point of origin.

Five different types of operation were employed in these 9 patients. These procedures are represented in Figure 2 as follows:

A. Anastomosis between the distal end of right superior pulmonary vein (proximal end ligated) and the side of the superior vena cava.

B. Division of the left innominate vein and anastomosis of its proximal end to the side of the left main pulmonary artery.

C. Division of the pulmonary artery to the right upper lobe and anastomosis of its proximal end to the side of the inferior vena cava.

D. Division of the pulmonary artery to the right upper lobe, anastomosis of its proximal end to the side of the superior vena cava, and anastomosis of its distal end to the proximal end of the right subclavian artery.

E. Division of the right main pulmonary artery, anastomosis of its proximal end to the side of the superior vena cava and anastomosis of its distal end to the proximal end of the right subclavian artery (this differs from "D" only in that it uses the main right pulmonary artery instead of the upper lobe branch).

It will be noted that type A establishes drainage of pulmonary veins into the vena cava whereas the other four types send blood into the cava from the pulmonary artery. Two of these procedures (D and E) have an additional connection between the two sides of the heart by way of the subclavian artery anastomosed end-to-end to the main right pulmonary artery or to its upper lobe branch.

One of these 9 patients died during operation. The 8 remaining survived completion of the operative procedure itself but all died subsequently. The time of survival varied from a few minutes to several days. In most cases pulmonary edema was the terminal feature. Two children in whom the pulmonary artery was anastomosed to the superior vena cava developed venous hypertension in the upper half of the body together with severe edema of the face. Although the arterial oxygen saturation in one of these patients rose to 82.4 per cent from the preoperative level of 39.5 per cent, he succumbed to pulmonary edema 30 hours after operation.

The fatalities in this group of patients suggest that the procedures employed are basically unsound in the treatment of transposition. On theoretical grounds one might doubt the advisability of performing shunts which would result in unbalancing the two sides of the circulation. It is to be recalled that the anatomical nature of complete transposition is such that blood coursing out of the right

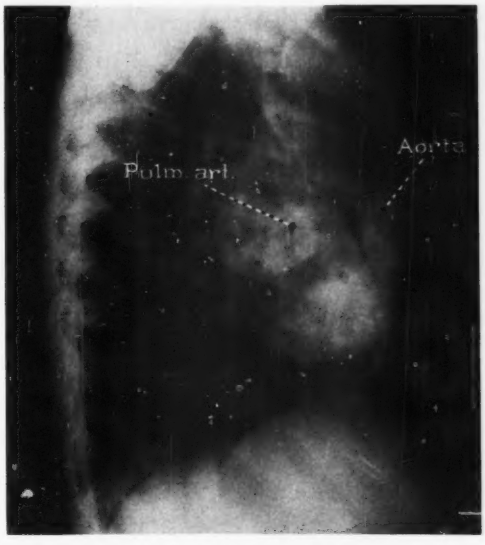

Fig. 1. Reproduction of an angiocardiogram in a patient with transposition of the great vessels. Note the characteristic anterior origin of the aorta. (Courtesy of Drs. Robert Cooley and Robert Sloan.)

ventricle is returned to the right auricle and that blood leaving the left ventricle through the pulmonary artery is returned to the left auricle. If postnatal survival is to occur in transposition of the great vessels, oxygenated blood must reach the aorta through some channel such as an auricular or ventricular septal defect. However, the volume of oxygenated blood shunted into the systemic circulation must be balanced by a similar volume of unsaturated blood entering the pulmonary circulation.

In a patient with transposition of the great vessels and a ventricular septal defect as the only compensatory mechanism, it is not unlikely that the shunt through the interventricular defect is a reversible one, with the direction of the flow dependent on relative pressures in the two ventricles. When the volume of blood on one side of the heart becomes significantly greater than that on the other side, the pressure rises on the side to which the blood has been shunted, causing a reversal of the shunt. The situation differs greatly from that in an uncomplicated patent ductus arteriosus, in which the blood shunted

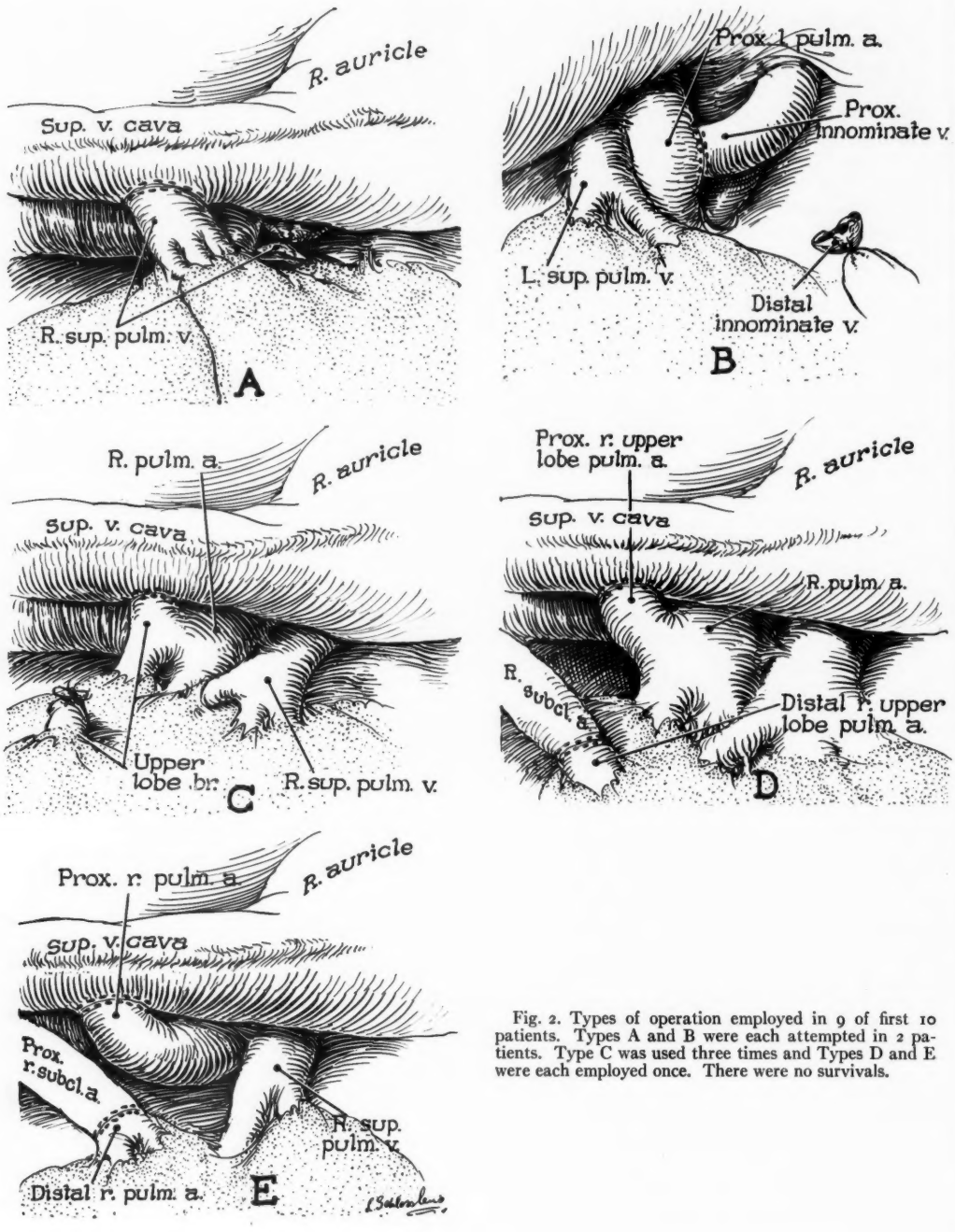

Fig. 2. Types of operation employed in 9 of first 10 patients. Types A and B were each attempted in 2 patients. Type C was used three times and Types D and E were each employed once. There were no survivals.

from aorta to pulmonary artery returns to the side of the heart from which it originated. In contrast to the shunt in transposition, the shunt in a patent ductus may remain unidirectional.

It seems apparent, therefore, that the therapeutic shunt in transposition should be effected if possible without unbalancing the circulation. This brings us to a consideration of auricular septal defect.

II. Creation of an auricular septal defect. It is well known that some patients with transposition of the great vessels and with an auricular septal defect as the only compensating abnormality may live for a number of years. It seemed reasonable to attempt to duplicate this beneficial effect by establishing artificial defects in the auricular septum in patients. Since every surviving patient with transposition has some type of abnormal communication between the systemic and pulmonary circulations it is necessary to exclude the likelihood of the presence of an adequate auricular defect before attempting to create one. We employed angiocardiography to determine whether a large interauricular communication existed; in none of these patients was a large defect demonstrated. We realize that even with angiocardiography it is difficult to be certain on this point, but in no case did the findings at operation suggest that a large existing septal defect had been missed during diagnostic tests.

We have previously described a method (2) for creating an auricular septal defect under direct visual control and without interruption of the circulation. The method depends on the fact that the proximal portion of the wall of the right pulmonary veins is adherent to the posterior wall of the right auricle. With appropriate occlusion of the lateral portion of the right auricle and of the right superior pulmonary veins one may excise a portion of the septum between the pulmonary veins and the right auricle, forming what is essentially an interauricular communication. After the defect is made, hemostasis is attained by suturing the edge of the incision in the anterior wall of the vein to the corresponding area on the lateral aspect of the right auricle. No sutures are required posteriorly.

Such a communication can be established quickly under direct vision and with little loss of blood. In addition to providing an avenue for exchange of blood between the auricles, it allows some blood returning from the right lung to flow directly into the right auricle. From this point it passes into the right ventricle and is ejected into the aorta. The remainder of the blood from the right lung together with that from the left lung, enters the left auricle to participate in the interauricular mixing previously mentioned.

The technique of operation is shown in the accompanying drawings. The chest is entered through the fourth intercostal space on the right and the azygos vein is doubly ligated and divided (Fig. 3). The pericardium is opened lateral to the phrenic nerve which is displaced medially. The right pulmonary artery and superior pulmonary veins are dissected free of the surrounding tissues. It is necessary to expose the pulmonary artery only enough so that it may be occluded temporarily during creation of the auricular septal defect. The superior pulmonary veins are exposed anteriorly from the lung to their point of adherence to the lateral aspect of the right auricle. A medial extension of this anterior dissection is to be avoided since it would produce an undesirable separation of the components of the auricular septum. Posteriorly, however, the dissection frees the veins well back toward the left auricle, so that the special occluding clamp may be placed far into the mediastinum.

With the pulmonary artery temporarily occluded by a long handled clamp, and the distal superior pulmonary veins occluded by a bulldog clamp, a special curved clamp is applied to the pulmonary veins and the right auricle as shown in Figure 4. The anterior blade of the clamp compresses the anterior wall of the right auricle against the auricular septum and the posterior blade compresses the posterior wall of the pulmonary veins against the septum. One may then incise the right auricle and the anterior wall of the superior pulmonary veins with negligible bleeding. These two incisions expose the lateral edge of the auricular septum which may be grasped with clamps and drawn outward as it is excised

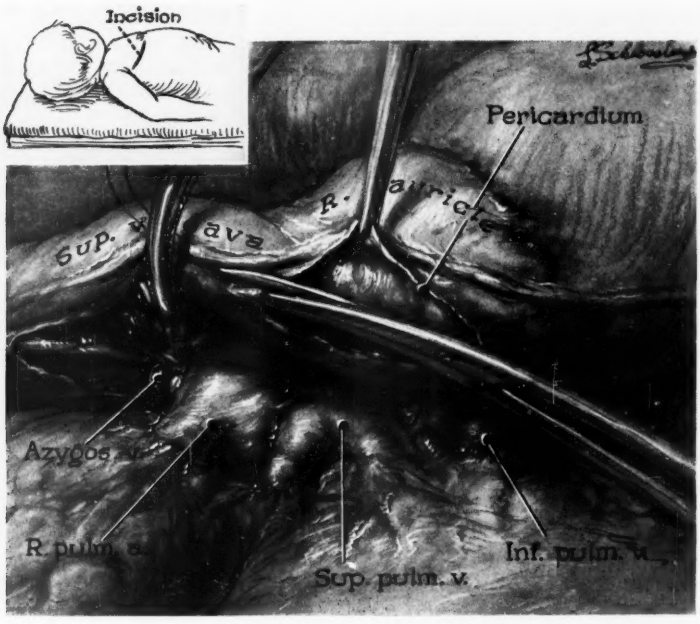

Fig. 3. Technique of creating an interauricular defect: Insert shows incision for entering chest through right fourth intercostal space. The azygos vein is divided and pericardium is opened lateral to the phrenic nerve. Note the large size of the pulmonary artery to the right upper lobe.

with scissors. Care should be taken to avoid cutting beyond the septum at the upper portion of the excision. If the excision is properly performed, one need only suture the anterior wall of the right auricle to the anterior wall of the superior pulmonary veins (Fig. 5). The special clamp is then released and the interauricular communication is established. The pericardium is loosely closed with a few interrupted silk sutures.

In the initial operations only the artery to the right upper lobe was occluded while the defect was being created. Since the patients in these early operations showed evidence of increased pulmonary engorgement on the right side, it was decided to occlude the entire right pulmonary artery during later procedures. This maneuver was well tolerated and seemed to lessen the tendency to pulmonary congestion.

Another maneuver which is helpful in the removal of a large portion of septum is the temporary release of the special occluding clamp. This enables one to draw the septum strongly outward and makes more septum available for excision. If the clamp is reapplied promptly there will be minimal loss of blood. Retraction of the edges of the remaining septum tends to make the defect slightly larger than the dimensions of the removed specimen. The appearance of the defect in situ is seen in the accompanying photograph and diagram (Fig. 6).

Twelve patients with transposition have been treated by creation of an auricular septal defect. Three have survived and seem to be improved. The 9 remaining died, most of them less than 24 hours after operation. It must be mentioned that many of these patients were in extremely poor condition; 1 was an 8 day old child who had been in an oxygen tent since birth. Detailed reports of the 3 surviving patients follow:

1. L.K.S. (H.L.H.—62951.) This 8 month old girl weighing less than 8 pounds entered the hospital on May 23, 1948. The chief complaints were cyano-

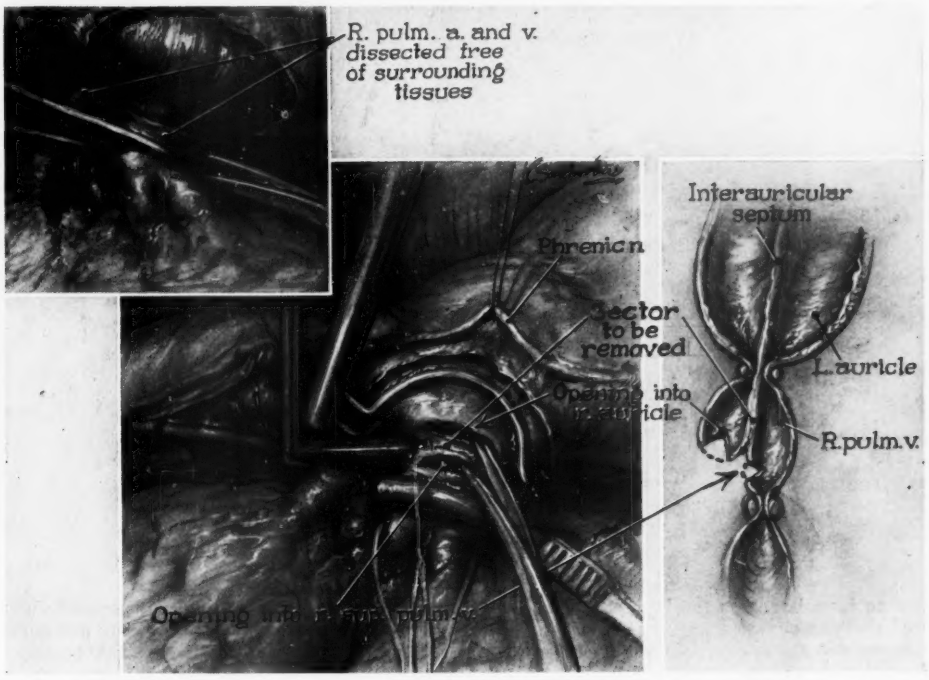

Fig. 4. Technique of creating an interauricular defect: With the pulmonary artery and superior pulmonary vein freed from the surrounding tissues (insert), the special clamp is applied to compress the right auricle and the superior pulmonary veins. Back-bleeding from the lung is prevented by the bulldog clamp on the distal pulmonary veins. The pulmonary artery is temporarily occluded to diminish pulmonary congestion caused by obstruction of venous out flow. An incision is made in the right auricle and in the superior pulmonary veins, exposing the lateral edge of the auricular septum for excision.

sis and dyspnea on exertion since birth, with anorexia and failure to gain and develop. Oxygen had been given continuously during the first 3 days of life and at night for the first 3 months. There had been no convulsions or loss of consciousness.

Examination revealed an undernourished, cyanotic child. The respiratory rate was 50 per minute at rest. The heart was enlarged but no murmurs were heard. The liver was considerably enlarged. There was pronounced clubbing of the fingers and toes.

The electrocardiogram revealed right axis deviation and right ventricular preponderance. The red blood cell count was 8.2 millions, hemoglobin 22 grams, and hematocrit 69. Fluoroscopy showed the heart to be greatly enlarged in the anteroposterior view with a full pulmonary conus. The base was narrow in the anteroposterior view and broad in the oblique views. There was a left aortic arch. The hilar markings were increased. X-ray findings confirmed the fluoroscopic examination.

On May 24, 1948 a thoracotomy was performed through the right fourth intercostal space. The pulmonary artery was large and thick walled and its pulsations were vigorous. The findings were typical of transposition. An interauricular defect was created. The child was discharged from the hospital 2 weeks after operation.

Several weeks later the red blood cell count had declined to 5.95 millions and the hemoglobin to 17.8 grams. The infant was alert and active but still somewhat cyanotic.

Sixteen months after operation the mother states that the child is improved but still has not been able to sit up. She weighs only 12¾ pounds and has just begun to take solid foods. Her color is better and cyanosis is not noticeably aggravated by crying.

2. K.D.L. (H.L.H.—60498.) This 2½ year old white girl entered the hospital on June 9, 1948 because of cyanosis and dyspnea since the age of 3½ weeks. She had experienced a number of urinary tract infections. Physical examination revealed a poorly developed cyanotic child weighing only 22 pounds. The pulse and respirations were rapid. There was a short, soft systolic murmur in the third interspace to the left of the sternum. The heart ap-

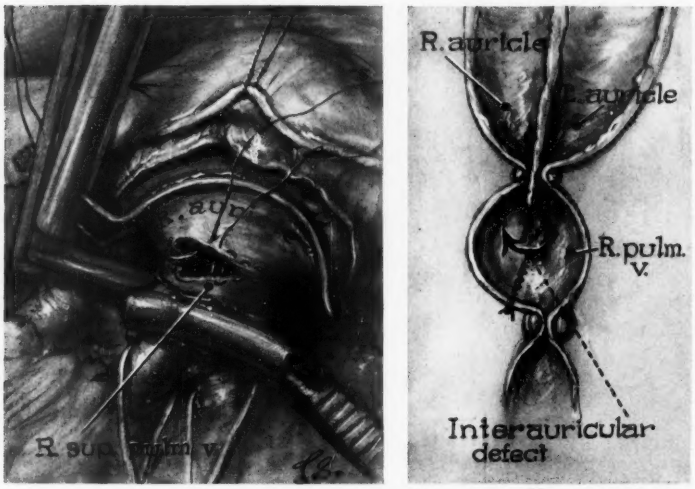

Fig. 5. Technique of creating an interauricular defect: The lateral edge of the septum has been excised and the right auricle is sewed to the anterior wall of the pulmonary veins. A cross-sectional view shows the relation of the defect to the edge of the septum.

peared to be enlarged to the left. There was advanced clubbing of the fingers and toes.

Fluoroscopic examination gave evidence of enlargement of both ventricles and the right auricle. The supracardiac shadows were narrow in the anteroposterior view and wide in the left anterior oblique view. There was a left aortic arch. There was evidence of congestion and increased pulsations in the lungs.

The arterial oxygen saturation was 54.1 per cent, the hematocrit 73, the hemoglobin 20.3 grams and the red blood cell count 8.85 millions. Electrocardiograms revealed a rate of 150, a *PR* interval of 0.15 second, and right axis deviation. The clinical impression was transposition of the great vessels with interventricular defect. This was confirmed by angiocardiography.

Operation was performed on June 10, 1948. The right pulmonary artery was thick walled and there were strong pulsations. The relationship of the pulmonary artery and the aorta was that of transposition. An interauricular defect was created.

The postoperative course was fairly stormy. Convalescence was delayed by the development of a urinary tract infection. The arterial saturation on July 7, 1948 was 71 per cent. She was discharged on that date in somewhat improved condition.

Examination 11 months after operation showed considerable improvement in exercise tolerance. She was no longer dyspneic at rest. The cyanosis was slightly improved and an oximeter reading at rest registered 81 per cent. This fell to 61 per cent after exercise. The red blood cell count and hematocrit were unchanged. The heart was no longer globular and the cardiothoracic ratio had decreased slightly from 56 to 52 per cent. She is to return in 6 months for consideration of an extracardiac shunt.

3. M.R. (J.H.H.—515459.) This 14 month old infant has been cyanotic since birth. She has developed slowly and weighed only 12 pounds, 15 ounces on admission to the hospital on September 26, 1949. Nine months prior to admission she developed a left hemiplegia which has cleared slowly since that time.

The findings on physical examination, on fluoroscopic examination, on catheterization and angiocardiography were indicative of a transposition of the great vessels. It was thought that there might be a very small interauricular defect. Red blood cell count, 9.8 millions; hemoglobin, 24 grams; hematocrit, 81.

Exploratory thoracotomy was performed on October 10, 1949 and findings typical of a transposition were noted. A large interauricular septal defect was created. There was no evidence of a previously existing defect. The patient's condition was rather precarious and an arterial anastomosis was not performed.

The patient's improvement in the short period since operation has been gratifying. The cyanosis has lessened and the appetite has improved considerably.

III. Creation of an auricular septal defect plus an extracardiac arterial shunt. It was proposed to anastomose one of the branches of the aorta to the right pulmonary artery after

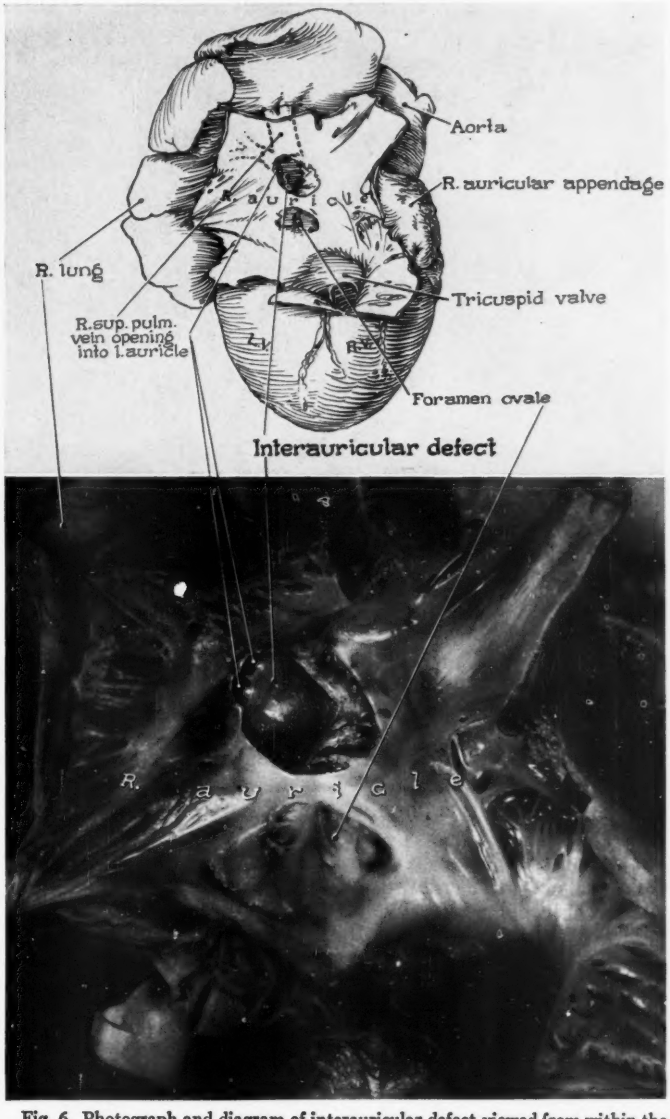

Fig. 6. Photograph and diagram of interauricular defect viewed from within the opened right auricle. The openings of the superior pulmonary veins and the dorsal wall of the left auricle may be seen through the defect.

completion of the interauricular defect. Since the pressure in the pulmonary artery is high in transposition, one cannot be certain that blood will flow from the systemic to the pulmonary circulation unless one interrupts a pulmonary artery or one of its branches and performs an anastomosis to its distal end. This is accomplished by division of the artery to the upper lobe of the right lung and anastomosis of the proximal end of the divided sub-

Fig. 7. Technique of anastomosis between proximal end of right subclavian artery and distal end of pulmonary artery to the right upper lobe. The subclavian artery is occluded proximally by a clamp and ligated distally preparatory to division. Note the suture line on the superior pulmonary veins marking point of closure after creation of interauricular defect.

clavian artery to the distal end of the pulmonary artery to the upper lobe (Figs. 7 and 8). In the presence of transposition this branch of the pulmonary artery is usually larger than the subclavian artery. A satisfactory end-to-end anastomosis is ordinarily possible.

A diagram of the circulation after creation of an auricular septal defect and end-to-end anastomosis between the proximal right subclavian artery and the distal pulmonary artery to the right upper lobe is seen in Figure 9. A large part of the additional blood sent to the right lung through the subclavian artery returns to the right auricle because of the auricular septal defect. This avoids the danger usually associated with a unidirectional shunt in transposition, since the septal defect acts to equalize pressure on the two sides of the circulation.

The double procedure has been carried out in 12 patients. All survived the operative procedure but 4 died shortly thereafter. One of these was a 6 month old infant in poor condition who had frequent bouts of cardiac arrhythmia during operation together with severe hemorrhagic edema of the right lung. He died 1 hour after operation. Two patients developed bloody diarrhea as the terminal event; one had appeared to be improved for several weeks until cardiac failure ensued. Detailed reports of the surviving patients follow:

1. M.J.R. (J.H.H.—427947.) This 3½ year old white boy was admitted to the Hospital on July 15, 1948 because of severe cyanosis and incapacity dating from birth. Despite hospitalization and almost constant oxygen therapy throughout the neonatal period he had three convulsions before the age of 3 months. Thereafter he had lost consciousness several times. Development was retarded and he weighed only 26 pounds on admission. He had not learned to walk until a month before entry.

Examination showed a small, cyanotic, underdeveloped boy with clubbing of fingers and toes. Respirations were 36 per minute, pulse, 108. The heart did not appear to be enlarged. There was a loud systolic murmur heard over all the precordium, maximal at the fourth left interspace.

Fluoroscopy showed marked "hilar dance." The supracardiac shadows were narrow in the anteroposterior view and wide in the left anterior oblique view. Red blood cells, 7.95 millions; hemoglobin,

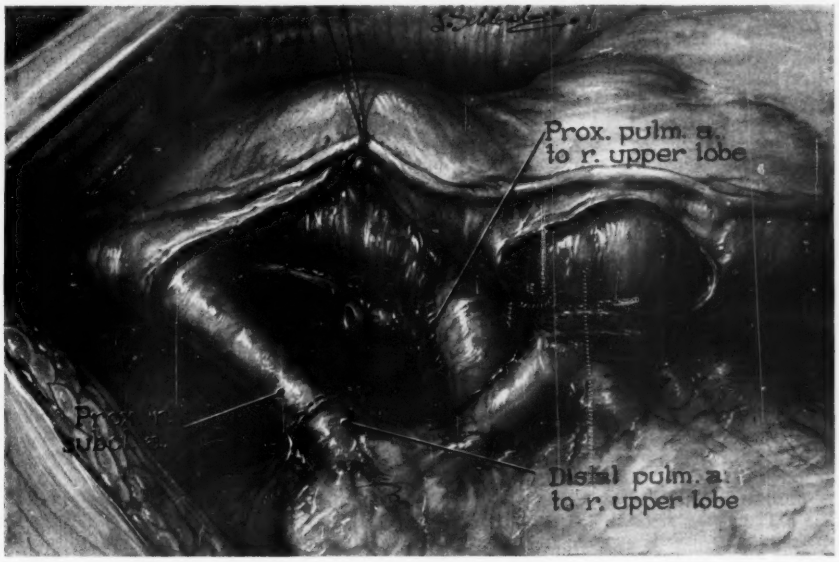

Fig. 8. The proximal pulmonary artery to the right upper lobe has been sutured after division. The proximal end of the right subclavian artery has been sutured to the distal end of the pulmonary artery to the right upper lobe.

17 grams; hematocrit, 61; arterial oxygen saturation, 42.5 per cent. Electrocardiogram showed right axis deviation and right ventricular hypertrophy. Angiocardiography confirmed the clinical impression of transposition of the great vessels.

A right thoracotomy was performed on July 23, 1948. The right pulmonary artery was tremendous in size and the pulsations were very strong. An interauricular defect was created. In addition, the proximal end of the right subclavian artery was anastomosed to the distal end of the pulmonary artery to the right upper lobe. The postoperative course was not unduly complicated. Laboratory studies 3 weeks following operation showed an hematocrit of 63, red blood cell count, of 7.5 millions, and hemoglobin of 20 grams. The arterial oxygen saturation was 53 per cent with the patient crying. His general condition seemed to be improved. He was discharged from the hospital on August 17, 1948.

In the 14 months since operation he has seemed to make steady progress. He is now very active, walks well, and does not appear cyanotic after exercise. A recent arterial oxygen saturation was 61 per cent with the patient crying. Because of severe symptoms associated with phimosis, a circumcision was performed on September 9, 1949, under cyclopropane anesthesia. This was well tolerated.

Although his general condition appears to be definitely better, it is worth emphasizing that the red blood count has risen to 9.0 millions with hemoglobin of 24.0 grams, and an hematocrit of 75.

2. J.H. (J.H.H.—380340.) This 7 year old white boy was first seen in the Cardiac Clinic in 1945 at the age of 4 because of persistent cyanosis since birth. At the time he was intensely cyanotic and undernourished and such was his condition on admission for operation on September 24, 1948. The patient was unable to walk but was able to stand without support. There was extreme clubbing of the fingers and toes. The chest was deformed. On fluoroscopic examination there was moderate cardiac enlargement which appeared to involve both ventricles. The supracardiac shadows were narrow in the anteroposterior view and wide in the left anterior oblique view. The aorta was large. There was a concavity in the pulmonary conus region. The vascular markings and the hilar pulsations were increased. The liver extended two finger-breadths below the costal margin. Angiocardiograms confirmed the clinical impression of transposition of the great vessels. There was no indication of a large auricular septal defect.

The red blood cell count was 8.5 millions, hemoglobin 25 grams and hematocrit 80. The arterial oxygen saturation was 42 per cent and 49 per cent on two separate occasions.

On September 28, 1948 an operation was performed through the 4th interspace on the right. There were vigorous pulsations in the pulmonary tissue. The right pulmonary artery was tremendous in size and its pulsations were very strong. The relationship of the aorta and the pulmonary artery was

that of a transposition. An interauricular defect was created. The proximal end of the right subclavian artery was then anastomosed to the divided distal end of the pulmonary artery to the right upper lobe.

The postoperative course was fairly smooth. The cyanosis was somewhat less than previously. The arterial oxygen saturation was 62 per cent, red blood cell count 9 millions, hemoglobin 22 grams, and the hematocrit 75 on October 28, 1948. He was able to walk six or eight steps without support and his strength seemed to be increasing when he was discharged on November 10, 1948.

He has been seen periodically since discharge and appears to be somewhat improved. Cardiac enlargement has not advanced but he has been maintained on digitalis. Eleven months after operation the red blood cell count was 9.3 millions with an hematocrit of 80.

3. R.D.C. (H.L.H.—65758.) This 2 year old white boy was admitted to the hospital on November 16, 1948, because of shortness of breath and cyanosis since birth. He was able to walk a short distance. Examination of the heart revealed a harsh precordial murmur which was loudest in the 4th interspace at the left sternal border. On fluoroscopic examination there was a definite concavity in the region of the pulmonary conus and increased hilar markings. Both the right and left ventricles were enlarged. The base of the heart was not particularly narrow. Angiocardiograms confirmed the clinical impression of transposition. The arterial oxygen saturation was 48.8 per cent, the hematocrit was 70.4. hemoglobin 23 grams and the red blood cell count 8.55 millions. Electrocardiogram indicated right ventricular hypertrophy.

Operation was performed on November 18, 1948, through the usual anterior incision in the fourth interspace on the right. The right pulmonary artery was greatly enlarged and the pressure was high. There were violent pulsations in the pulmonary tissues. An interauricular defect was created and the proximal end of the right subclavian artery was anastomosed to the divided distal end of the pulmonary artery to the right upper lobe.

The patient's convalescence was complicated by the development of chicken pox. He seemed to be improved at the time of discharge despite the fact that the blood oxygen values were about the same as before operation. The arterial oxygen saturation was 47.0 but he was struggling at the time that the arterial puncture was performed. The hematocrit was 56 and the hemoglobin 17 grams at discharge.

Eight months after operation the hemoglobin was 20 grams and the hematocrit 66. These figures indicated a rise since the time of discharge, but they are still below the preoperative level. Ten months after operation the patient's parents state that he is very much improved. They have great difficulty in restricting his activity. There is no dyspnea but some stridor, which may be due to tracheal compression by an anomalous vessel. This point is to be investigated.

4. G.C. (J.H.H.—449266.) This 7 year old white girl was admitted to the hospital because of cyanosis and intolerance to exercise. The clinical impression was transposition of the great vessels. This was confirmed by angiocardiography and cardiac catheterization. The red blood cell count was 9.2 millions, the hemoglobin 23 grams and the hematocrit 72. The arterial oxygen saturation was 67 per cent.

Operation was performed on April 7, 1949 by the usual approach. The right pulmonary artery was large and thick-walled but the pressure seemed to be less than in the usual transposition. It was measured at only 300 millimeters of water. However, the aorta appeared to arise from the right ventricle which substantiated the diagnosis of transposition. A large interauricular defect was created. Since the pressure in the aorta was obviously higher than that in the pulmonary artery, an anastomosis was performed between the proximal end of the subclavian artery and the side of the right pulmonary artery rather than the usual type of anastomosis of the subclavian artery to the distal end of the pulmonary artery to the right upper lobe.

Her postoperative course was smooth. The arterial oxygen saturation rose to 80 per cent and she was obviously improved. She was discharged from the hospital 20 days after operation in excellent condition. It is not improbable that this patient had pulmonic stenosis as well as transposition of the great vessels.

Six weeks after operation she was able to walk twice as far as before without dyspnea or increase in cyanosis. The hemoglobin at that time was 17.5 grams, the red blood cell count 6.97 millions and the hematocrit 54.

Five and a half months after operation the patient seemed to be improving steadily with increased tolerance for exercise. The hemoglobin was 17 grams, the red blood cell count 6.36 millions, and the hematocrit 51. The arterial oxygen saturation was 75.4 per cent with the patient crying.

5. C.R.S. (H.L.H.—58356.) This boy was first seen in the Harriet Lane Cardiac Clinic in October, 1947 at the age of 34 months. He had been cyanotic since birth and his development was greatly retarded. Examination showed a fairly well developed cyanotic child with clubbed fingers and toes. The heart was enlarged to the right and left with a harsh systolic murmur over the precordium. The electrocardiogram indicated right ventricular hypertrophy and right axis deviation. The red blood cell count was 7 millions with an hematocrit of 56.8. A tentative diagnosis of transposition of the great vessels was made.

He returned in June, 1949, weighing only 30 pounds. He was not yet able to walk. Examination of the cardiovascular system was unchanged except that the hilar markings were prominent and could be seen to pulsate. The red blood cell count had risen to 9.25 millions with an hematocrit of 75. Oximeter test showed a resting arterial oxygen saturation of 44 per cent.

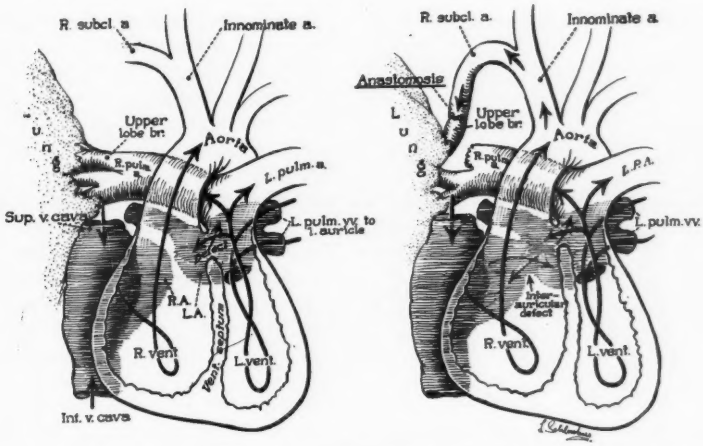

Fig. 9. a, left, Transposition of the great vessels before surgical intervention. Diagram shows crosscirculation through the interventricular defect but the auricular septum is intact. b, Diagram showing conditions after formation of interauricular defect and extracardiac shunt from right subclavian artery to upper lobe of right lung. The interauricular defect permits two-way flow between the auricles.

The diagnosis of transposition was confirmed at operation on June 21, 1949. An interauricular defect was formed, followed by anastomosis between the proximal end of the right subclavian and the distal end of the pulmonary artery to the right upper lobe.

He was discharged from the hospital on July 18, 1949 after an uncomplicated course. One week later his red blood count was 8.8 millions and hematocrit 65. The resting oximeter reading was only 50 per cent but he appeared to be improved in color. Two and one-half months after operation he is walking fairly well, has gained 2½ pounds and the parents feel that he is distinctly improved.

6. V.B. (A–49336.) This white girl was first seen on July 26, 1946 at the age of 3 years and 9 months. She had been cyanotic since birth and had suffered three spells of unconsciousness since November, 1945. There was moderate decrease in exercise tolerance. Examination showed an alert child with cyanosis and clubbing of the extremities. The heart was not enlarged. There was a loud systolic murmur over the entire precordium. The hilar markings were prominent and expansile. There was a right aortic arch. The electrocardiogram showed right axis deviation. The red blood cell count was 9.43 millions with an hematocrit of 71. The arterial oxygen saturation was 54.2 per cent.

She returned on August 2, 1949. There had been no restriction of exercise but she tired readily and squatted frequently after the slightest exertion. She could walk half a block or climb one flight of stairs. There was a chronic mild productive cough. The cardiovascular findings were as before; the liver was just palpable. Red blood cell count was 10.45 millions and hematocrit 83. Angiocardiography confirmed the clinical impression of transposition of the great vessels.

On August 13, 1949, an interauricular defect was created followed by the usual anastomosis between the right subclavian artery and the branch of the pulmonary artery to the right upper lobe. Her response to operation was good but she soon developed a spiking fever which failed to respond to any of the antibiotics. Despite many blood cultures and intensive clinical and laboratory study the cause of her fever was not certainly ascertained, but she became afebrile 6 weeks after operation. Since she is just beginning to resume activity it is too early to evaluate the clinical result. The red blood cell count had dropped to 7.3 millions with an hematocrit of 62 on September 18, 1949.

7. M.B. (J.H.H.—513342.) This 4½ year old white boy was noted to be cyanotic several months after birth. At the age of 6 months he became unconscious momentarily and 1 month later suffered a right hemiplegia which had only partially cleared at the time of entry. Examination showed a maldeveloped, cyanotic boy with clubbed digits and residua of a right hemiplegia. Examination showed enlargement of both sides of the heart and other findings typical of transposition of the great vessels. Angiocardiography confirmed this impression. The electrocardiogram showed an incomplete bundle branch block. The red blood cell count was 10.35 millions with an hematocrit of 82. The resting oxygen saturation was 47 per cent by oximeter.

On September 16, 1949 the usual auricular septal defect and subclavian to pulmonary artery anastomosis was performed. His course since operation has been smooth, and he seems to be improved.

8. T.F.H. (J.H.H.—515062.) This 4½ year old white boy was born cyanotic and developed very poorly. He entered the hospital on September 20, 1949. Examination showed a moderate enlargement of both sides of the heart with a clinical and angiocardiographic picture of transposition of the great vessels. There was a definite hydrocephalus but this did not appear to be progressive and he showed no obvious mental retardation. The red blood cell count was 9.5 millions with an hematocrit of 81.

On September 28, 1949, an interauricular defect was created followed by anastomosis of the proximal subclavian artery to the distal end of the pulmonary artery to the right upper lobe. His immediate course since operation has been uncomplicated and he shows evidence of being considerably improved.

DISCUSSION

In transposition of the great vessels the left ventricular output through the pulmonary artery returns to the left auricle and the right ventricular output through the aorta returns to the right auricle. Survival of a patient with this abnormality is dependent on the existence of some type of communication between the two circulations so that oxygenated blood from the lungs may be sent to the tissues of the body. Equally important is the transfer of unoxygenated blood to the pulmonary circulation, since a unidirectional shunt would lead to depletion of the donor side of the circulation.

Interauricular defects or interventricular defects permit such an interchange between the two sides of the heart. Whether the flow through such defects is simultaneously in both directions or is an alternating one need not concern us here. It is apparent on theoretical grounds that the facilitation of intracardiac mixing should benefit the patient with transposition, whereas unidirectional shunts would be poorly tolerated. Supportive evidence for this concept is furnished by the results in the patients reported here.

In 9 patients with transposition an extracardiac shunt between the two sides of the circulation resulted fatally in all instances. However, as there were 5 types of extracardiac shunt and no one type was used more than 3 times, the fatal results do not necessarily establish each type of procedure as unsound. The possibility of technical failure to account for a specific bad result must be kept in mind. Furthermore, most of these patients were in very poor condition at the time of operation.

In 12 patients submitted to operation for the production of an interauricular defect there were 9 deaths, some due to technical factors which have no bearing on the theoretical basis for such a procedure. The 3 survivors are improved, although not dramatically so.

The highest percentage of survivals has occurred in the group with a combination of intracardiac and extracardiac shunts. There were 4 deaths among 12 patients in whom an interauricular defect was created together with an anastomosis between the subclavian and pulmonary arteries. Most of the survivors seem to be improved which establishes this as the most successful method we have employed. It should be noted, however, that in patients tolerating operation poorly the procedure is generally terminated after the creation of an auricular septal defect, whereas patients in better condition are subjected to an extracardiac shunt at the same operation. Best results have been obtained after the combined intracardiac and extra-cardiac shunt, which would be expected to be most beneficial according to our present theory.

The most striking improvement was noted in patient No. 4 of the group in which an interauricular defect and an extracardiac arterial shunt were created. This patient probably had mild pulmonic stenosis as well as transposition of the great vessels. The gratifying result at least raises the question as to whether one should attempt to constrict the pulmonary artery prior to carrying out the other operative procedures in patients with transposition of the great vessels.

One disquieting aspect of surgical therapy is the fact that a number of the survivors are only moderately improved. In the treatment of tetralogy of Fallot many of the survivors are restored to essential normality as far as activity is concerned; after treatment of transposition the degree of activity is not so dramatically increased. Moreover, the arterial oxygen saturation generally remains below 75 per cent so that the stimulus to polycythemia persists. In some instances the red blood cell count has become higher after operation than it was before.

These considerations suggest that some different surgical attack should be employed. The most direct approach would disconnect the aorta and pulmonary artery from the heart and reattach them to their proper ventricles. A similar result might be achieved if the aorta and pulmonary artery were connected by the use of arterial grafts. Even were this latter maneuver accomplished in patients, the coronary arterial circulation would still arise near the origin of the aorta which receives poorly oxygenated blood from the right ventricle. However, with the transposition surgically treated, the oxygen content of the right ventricular blood should rise somewhat so that the cardiac musculature would be supplied adequately with oxygen.

On the other hand, the arterial side of the circulation could be left intact and the veins could be transposed. The multiplicity of veins and the decidedly less favorable results in venous anastomoses make this prospect a discouraging one. As an additional somber note on corrective measures in general, there is some doubt as to the recuperative power of pulmonary tissue which has been exposed to a very high arterial pressure for an extended period.

Many of the difficulties enumerated should yield to progressive technical advances. For example, the further development of devices to replace the pumping action of the heart and the oxygenating function of the lungs may permit definitive plastic surgery of the type necessary to transpose the great arteries or veins. Our current practice of altering physiology favorably by adding further anatomic abnormalities could then give way to true anatomic restorations.

SUMMARY

The diagnosis of transposition of the great vessels has been considered briefly and our attempts at surgical correction have been described.

Thirty-three patients have been treated (1) by some type of extracardiac venous or arterial shunt, (2) by the creation of an auricular septal defect, or (3) by a combination of these two methods. The combined procedures seem to offer the greatest likelihood of improvement.

Whereas most of the patients have survived the operative procedure itself, the postoperative mortality has been high. Most of the deaths are attributable to the precarious condition of the patients, to the use of procedures now considered unsound, or to technical errors. In the first 28 patients upon whom we operated for transposition, there were 22 deaths. This exceedingly high mortality has been lowered somewhat by the survival of the last 5 patients.[1] In the total of 12 patients treated by the creation of an auricular septal defect and an anastomosis between the right subclavian and pulmonary arteries, 8 are living with various degrees of improvement.

It is to be hoped that an operative procedure will be perfected which will produce a true anatomic correction of the defects rather than the partial physiological readjustment which has been accomplished in some of our patients. Experiments directed to this end are being continued.

[1]Furthermore, the succeeding 4 patients survived the operation and show evidence of improvement.

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COMBINED RADICAL CERVICOFACIAL PROCEDURES FOR PRIMARY FACIAL CANCER

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THERE are certain primary cancers of the lateral portion of the head (face) which, by their anatomical relation to local pathways of lymphatic drainage, may present a pattern of almost continuous metastatic nodal involvement from the primary site to the clavicle. Thus local excision of the primary neoplasm, though performed in radical fashion and followed some time later by block dissection of the neck, may ultimately represent surgical frustration because of the subsequent development of cancer in the undissected area separating the two operative fields.

The lateral areas of the face, including the temporal portion of the scalp, and notably the preauricular and postauricular areas as well as the auricle itself, are those in which these neoplasms occur. From these sites a continuous chain of lymphatic metastases may develop, first in the local periauricular nodes, then spreading in an almost arborescent pattern around or even within the cervical tail of the parotid gland, and thence into the adjacent submandibular lymph nodes. Those primary lesions located in or anterior to the auricle are thereafter more prone to metastasize from this area into the anterolateral triangle of the neck, while those of retroauricular origin extend also into the posterior cervical triangle.

The malignant neoplasms ordinarily encountered in these areas and capable of such a metastatic spread are usually cutaneous in origin. Squamous carcinoma is the most frequent, while melanoma constitutes an even more urgent indication for radical surgical measures. Some of the frankly malignant variants of so-called mixed salivary gland tumors of the parotid may occasionally behave in the same fashion. The sarcomas of connective tissue origin, because of their infrequent dissemination by local lymphatic routes, are ordinarily suitable for local extirpative measures.

In the instance of squamous carcinoma, a recognition of certain limitations of radiation therapy as a curative agent is important: the presence of actual invasion of bone or cartilage by the neoplasm, or the presence of local or cervical lymph adenopathy presumably of metastatic nature. The radiosensitive neoplasm becomes radioresistant in an osseous or cartilaginous bed, and even if destroyed therein by irradiation, the sequelae of radiation necrosis, sequestration, and painful osteitis or chondritis are so likely that the risk is unwarranted. Squamous carcinoma is also refractory to irradiation in lymphnodal deposits and radical surgery is the only definitive prospect for cure. Here the surgeon encounters a form of malignant neoplasm the caudad spread of which is usually limited by the floor of the supraclavicular space. If technical and biological operability can be established, cure may be achieved even in the presence of bulky cervical metastases.

A large proportion of malignant melanoma will have metastasized beyond the local and cervical areas of lymph node drainage before treatment, as in other anatomical primary sites. For the small potentially curable fraction radical local excision and block dissection in its most drastic possible form offers the only effective means of cure at present. Melanoma occurring in the area under discussion can be so attacked more efficiently than in most other sites, and certainly more effectively than similar lesions which are primary in extremities.

Effective surgical treatment of these neoplasms should embody the same principles of cancer surgery applied in such anatomical areas as the breast. This implies a certain disregard for the niceties of cosmetic end result. Adequate extirpation of the primary lesion may require sacrifice of a large area of skin,

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with the deep plane of removal at the level of periosteum or muscle fascia. Extensive lesions of the ear will require its entire removal, sometimes with wide exposure of the mastoid or even mastoidectomy. Primary lesions of the external auditory canal (squamous carcinoma) may extend into the middle ear and require its ablation. Although these neoplasms do not invade the mandible as do intraoral carcinomas, a few of them will invest the ascending ramus or become attached to it, so that mandibular resection with temporomandibular disarticulation will be a necessary part of the operation.

In certain instances the resulting defect in the area of the primary lesion can be reconstructed by the use of sliding flaps of adjacent skin or scalp, less commonly by immediate split or full thickness skin grafts. Large defects may be partially closed by sliding flaps, with secondary reconstruction at a later date when clinical control of the lesion seems assured. In older individuals, and particularly with the loss of all or part of the auricle, present day prosthetics offer a more rational solution than does plastic surgery.

Regional block dissection to accomplish removal of the lymphatic pathways of extension is the essential feature of the surgical procedure as an effort to achieve curative end results. The extent of the cervical block dissection should be as wide and as radical as is consistent with a reasonably low postoperative mortality and minimum impairment of function. Advanced age and severe concurrent organic disease offer the only hazards to a low operative mortality in these procedures, other factors being favorable. Surprising functional end results are possible with the loss of many structures in the neck which the surgeon may attempt to save only to sacrifice the effectiveness of the entire procedure. The removal of the internal jugular vein and sternocleidomastoid muscle should be a part of standard procedure in any cervical dissection, for their preservation decreases greatly effective cleanout of the neck. The cervical tail of the parotid, and that portion of the gland adjacent to the angle of the mandible, are best removed to obtain a satisfactory en bloc removal between the cervical and facial portions of the procedure. In this area the main portion of the fifth nerve lies deep to the excised portion of the parotid, in which we have twice demonstrated intraglandular extension of squamous carcinoma situated more cephalad.

Other structures in the neck may require removal because of proximity or attachment to gross lymphnodal metastases. The eleventh nerve has repeatedly been resected with little functional disturbance. Removal of the digastric bellies and omohyoid muscle, resection of the scaleni are followed by no untoward sequelae. In fact, with extensive cervical metastases one's concept of operability will be liberalized by forgetting the meticulous delicacy of classical anatomical dissection and emphasizing those few structures which require preservation. The common and internal carotid arteries, the vagus, phrenic, lingual, and hypoglossal nerves represent the vital anatomical landmarks to be preserved intact. In 3 patients, as a planned procedure, and with prior, intermittent pressure, the common carotid artery has been resected with cerebral damage in 1 of the 3 cases.

The exact limits of the neck dissection are determined by the location of the primary lesion. In general, lesions preauricular require complete block dissection of the anterolateral triangle. When the auricle or adjacent skin is the primary site, the line of the anterior border of the sternocleidomastoid represents the linear axis of the cervical operative field, and the dissection should be carried forward into the anterolateral area, and posteriorly into the posterior triangle to the degree indicated by the nature and extent of the neoplasm, or as permitted by the age and physical condition of the subject. A melanoma in a young individual, for example, should be an indication for a cervical dissection of the most radical sort. Lesions originating in the postauricular zone require wide dissection of the posterior triangle, with inclusion of the lateral portion of the anterolateral triangle in the operative field.

In conformance with the principles of extirpative surgery for cancer, the dissection should begin at the level most distal from the primary site, or at the floor of the supraclavicular space. In the instance of melano-

Fig. 1. Case 1. J.H., 5 years postoperative; extensive squamous carcinoma of ear with infiltration of external auditory canal and a continuous chain of metastases from preauricular to supraclavicular nodes.

Fig. 2. Case 2. W.G.M., 2 years postoperative; squamous carcinoma helix of ear with involvement of retroauricular and submandibular nodes.

mas, this should include unroofing of the superior pulmonary sulcus with exposure of the apical portion of the lung. The sternocleidomastoid muscle is divided at its origin, and the internal jugular vein resected near its junction with the subclavian. The sheath of the carotid artery is removed by sharp dissection, and all of the loose connective and areolar tissue in the carotid compartment meticulously removed. The submaxillary triangle and the adjacent submental space is cleaned out for preauricular lesions, while only the posterior portion of the submaxillary space need be dissected for postauricular neoplasms.

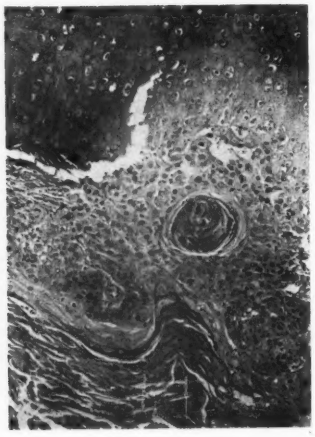

Fig. 3. Case 2. Photomicrograph showing squamous carcinoma infiltrating cartilage.

As the dissection is carried upward before or behind the ear, skin flaps should be reflected anteriorly or posteriorly to permit wide dissection down to the parotid capsule in the cheek, to the cartilage of the ear, to the periosteum of the mandible. Posteriorly, the ear may be dislocated medially while the retroauricular dissection is accomplished.

The procedure is completed by wide elliptical incisions around the primary lesion, reflection of skin flaps and finally radical removal of the primary tumor in one continuous block with the products of the preceding dissection. In some instances when closure is not possible, when the neoplasm is ulcerating and infected, or when there is periosteal or osseous involvement, cautery destruction of the primary tumor itself may be a superior technique. Such resulting defects will exhibit remarkable healing and may or may not require subsequent plastic repair.

Of 13 patients who have presented this specialized problem in the past 5 years, 6 have had squamous carcinoma primary in the auricular skin, 4 in the skin adjacent to the ear. Two had primary melanoma of the temporal

Fig. 4. Case 3. F.T., 3 months postoperative; melanoma primary at *X*, with metastases to submandibular and midcervical nodes.

Fig. 5. Case 3. Surgical specimen showing area of primary lesion, regional nodes, and products of neck dissection in continuity.

skin and 1 patient had a thrice recurrent salivary gland tumor which had histologically evolved into a pattern of almost pure adenocarcinoma. The patients were seen at the Los Angeles County Hospital or in the author's private practice. One patient, past 70 years of age, died of surgical shock 24 hours after operation, the only postoperative death. Neither the number of patients or the elapsed postoperative time is adequate to permit any dalliance with statistics.

The following illustrative cases are typical.

CASE 1. J. H., white male, aged 62 years, was first seen in February 1942, with the major portion of the right auricle replaced by an ulcerating, grossly infected cancer. There was a continuous chain of hard, enlarged nodes up to 3 centimeters in diameter from the preauricular to the supraclavicular areas. Biopsy of the primary lesion showed squamous carcinoma, Grade III. At operation, an involved node was found behind the clavicle; there were multiple deep cervical nodes enlarged, and extensive submaxillary node disease. The entire ear was removed, the external auditory canal found to be infiltrated requiring cautery destruction which was carried over the adjacent surface of the mastoid. Microscopic examination showed all of 12 to 15 nodes examined replaced by carcinoma. Two months later a rapidly growing, fungating recurrence appeared at the lower edge of the operative defect at the site of the ear. Wide cautery destruction was done. Subsequently there was repeated sequestration of portions of the mastoid process, and the defect finally became healed in 1944. Last seen in September, 1946 with no evidence of disease and no complaints. Reported by letter in September, 1948 from Oklahoma that he is still well, 6½ years after operation.

CASE 2. W. G. M., a 55 year old white male, was first seen in March, 1946. He had been treated by x-ray in January and February, 1946, 3200 roentgens at 80 kilovolts, unfiltered, in fractionated dosage. He presented a 2.0 by 1.0 centimeter deeply ulcerating lesion on the helix of the right ear, with exposed cartilage and edema and chondritis producing severe pain. The preirradiation biopsy had shown squamous carcinoma, Grade II. There were postauricular hard nodes 1 to 2 centimeters in diameter, and a 2 centimeter hard, right submandibular node. Radical dissection of the right anterolateral triangle was done and a Y incision made with preauricular and postauricular incisions. The uninvolved lobe and tragus of the ear were dislocated upward and anteriorly, permitting dissection of the periauricular nodes and wide resection of the involved portion of the ear. Microscopic sections showed deep invasion of cartilage by the tumor in this patient. He died 2 years later without evident recurrence, following gastric resection for ulcer.

CASE 3. F. T., aged 35 years, first consulted a physician in May, 1946 because of a tumor in the left side of the neck of 6 weeks' duration. The physician obtained a biopsy which showed metastatic melanoma in lymph node. Examination revealed a 1.0 by 1.5 centimeter smooth, dark brown lesion in the left temporal skin, and on inquiry the patient stated that this mole had doubled in size in the preceding several months. In the left submandibular space was a firm 3 by 2 centimeter node with a well healed recent incision in the overlying skin. There

were 6 to 8 palpable nodes up to 2 centimeters in diameter in the carotid and supraclavicular triangles. Other physical examination and x-ray films of the chest were not significant. The patient was immediately admitted to the hospital and block dissection of the entire anterolateral and posterior triangles was done, exposing the apex of the lung in the base of the wound, with en bloc dissection of the preauricular nodes, excision of the temporal fascia beneath the primary tumor. The gross specimen measured 28 centimeters in length, 10 centimeters in its greatest width, and 5 centimeters in maximum depth. Sixteen lymph nodes other than the large submandibular node were found, and only 1 of these showed metastasis on microscopic examination. The patient returned to his work as a truck driver in 4 weeks, and was well until April, 1947, at which time a roentgenogram of the chest showed bulky mediastinal enlargement, with death occurring 2 months later. The head and neck showed no evidence of recurrence.

SUMMARY

Certain malignant neoplasms (squamous carcinoma, melanoma) originating in the auricle or adjacent skin, usually disseminate locally by continuous lymphatic spread through the auricular and periparotid and submandibular nodes to the deep cervical nodes. Their cure demands a combined radical cervicofacial procedure, with en bloc removal of the primary tumor, the local nodes, and the products of block dissection of the neck.

PREMALIGNANT LESIONS OF THE AMPULLA OF VATER

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IN a recent survey of tumors of the pancreas at the Lahey Clinic from January 1, 1942 to January 1, 1949, 175 cases were studied. All of these patients were submitted to surgery. Of this group there were 165 cases of carcinoma of the ampulla, head, body, and tail of the pancreas, duodenum, and lower common bile duct. In the remaining 10 cases the tumors were benign. In this latter group 2 benign papillomas of the ampulla were found and the patients were submitted to surgery with a tentative diagnosis of carcinoma of the ampulla. In the series of carcinomas there were 59 radical resections for carcinoma of the head, or ampulla, duodenum, or lower common bile duct. In 4 of these cases the carcinoma originated in a lesion considered premalignant, such as a papilloma, polyp, or an adenoma. We wish to present the 2 cases of benign papilloma of the ampulla, and the 4 cases of carcinoma originating in a benign lesion in detail in order to emphasize the importance of these benign lesions in this region. We will show that such lesions produce symptoms of obstruction of the common bile duct; that they are not uncommon, a fact emphasized by Baggenstoss from the Mayo Clinic; that they are certainly premalignant; and that the malignancy which arises in these lesions may be curable by radical pancreatoduodenectomy.

LITERATURE

There have been few reports dealing with benign lesions of the ampulla of Vater. Christopher, in 1933, reviewed the literature and collected 41 cases of benign tumors involving the extrahepatic bile passages. He stated that such lesions were extremely rare. In his collected series there were 16 papillomas and polyps, 15 adenomas, isolated examples of lipoma, fibroneuroma, granuloma, melanoma, and carcinoid. In 6 cases of this reported series the tumor definitely involved the ampulla. He added a case report of an adenoma to this collected series.

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Archibald, in discussing Bazin's presentation of a benign polyp of the common duct, presented a personal case of a female patient who had a cholecystectomy which was followed by nausea, vomiting, and painless jaundice. In this case Archibald found at operation a moderately dilated common duct without stones in the common duct. The probe passed easily into the duodenum. He then performed duodenotomy and found a tiny papilloma of the ampulla protruding into the lumen of the duodenum.

In 1938 Baggenstoss reviewed the literature on benign lesions of the papilla of Vater. He reported 25 cases of polyps of the major duodenal papilla encountered at the Mayo Clinic. All of these lesions were found incidentally at autopsy. In the histories of 6 patients, he found symptoms referable to the major duodenal papilla had there been no complicating lesion such as cholecystitis, cholelithiasis and duodenal ulcer. He stated that these cases suggested that inflammation and irritation of the mucosa of the papilla played a part in the appearance of polypoid hyperplasia.

Baggenstoss suggested several etiologic factors for such neoplasms at the ampulla. In his series the mean age of the patients was 55.1 years. He believes that the increase in age is associated with a probable decrease of normal inhibition of cellular hyperplasia or neoplasia. In 23 of 25 cases there were neoplasms elsewhere, of which 9 were malignant and 14 benign. Since several types of epithelium meet at the papilla, and this region is stimulated by a variety of digestive enzymes and chemical substances, it becomes an ideal situation for neoplasms to develop, that is, an area of epithelial transition which is constantly being irritated chemically and mechanically. In his study he noted a striking resemblance of papillomas to low grade papil-

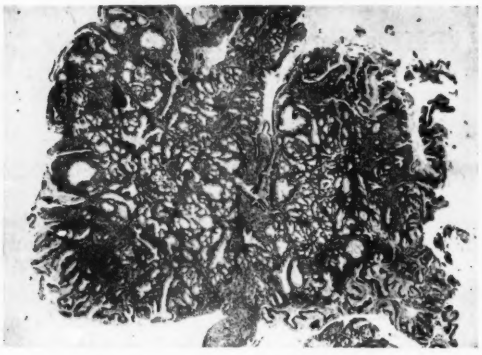

Fig. 1. Papilloma excised in Case 2, demonstrating the typical microscopic appearance of a papilloma as well as adenomatous hyperplasia.

lary carcinoma of the ampulla. Furthermore, he quoted Bell who stated that the distinction between the early stages of cancer and inflammatory hyperplasia is often an arbitrary one. Finally, Baggenstoss found 4 polyps of the major duodenal papilla in 100 consecutive autopsies in which a careful search of this area was made.

Baggenstoss concluded from this experience that because of the structural peculiarities of the major duodenal papilla, inflammation of this structure may give rise to symptoms and sometimes will produce jaundice. Polyps of this region have the same significance as polyps elsewhere. They may produce obstruction to the common duct and are related to cancer as premalignant lesions.

The abstracts of our cases which follow will serve to direct attention to benign lesions of the ampulla as a possible source of malignant disease, as a possible source of symptoms relative to the extrahepatic biliary tree and, finally, as a possible cause of symptoms which recur following cholecystectomy.

CASE REPORTS

CASE 1. This 53 year old housewife was first seen at the clinic February 23, 1944. She had been well until December 1943 when she had an episode of nausea with vomiting after which she had taken only liquids for several days. When the diet was increased to include solid foods, she experienced a cramping pain in the epigastrium which lasted approximately 5 hours and which was somewhat relieved by vomiting. Much later in January, she had another attack of epigastric pain which was accompanied by jaundice. A third attack followed a month later in February which was severe, lasted approximately 12 hours, and which was relieved by morphine; epigastric soreness, however, persisted. This attack also was accompanied by jaundice and 4 days after the onset, she began to menstruate, something she had not done for over a year and a half. She had lost 24 pounds in 2 months.

On physical examination the patient was slightly jaundiced; the abdomen was tender in the left lower quadrant, no masses were palpable and the liver was not palpable, but on subsequent examination there was thought to be a tender mass in the left adnexal region. The impression after this preliminary examination was that she had either a common duct stone or possibly a malignant tumor of the ampulla

The patient was admitted to the hospital. The hemoglobin on admission was 11.9 grams, erythrocytes numbered 3,820,000, leucocytes 7,100, the differential count was normal, nonprotein nitrogen was 35 milligrams, and the serum bilirubin was 5.8 milligrams per 100 cubic centimeters. The urine and stool contained bile.

On February 29, 1944, an exploratory operation was performed and a tumor approximately 1 centimeter in diameter was felt through the duodenum at the ampulla of Vater. It was thought that this tumor was malignant. There was moderate dilatation of the common bile duct. *The gall bladder was not dilated.* She was considered a poor surgical risk even though her disease was only of 2 months' duration. Therefore, a two stage resection was planned and a preliminary cholecystjejunostomy was done. The postoperative course following this initial stage was uneventful; the serum bilirubin fell to 0.6 milligram per 100 cubic centimeters on March 6, 1944.

On March 18, 1944, eighteen days after the first stage operation, the second operation was performed; it was planned to do a second stage pancreatoduodenectomy at this time. After mobilizing the duodenum and the head of the pancreas, the ampulla was accurately palpated and a 4 millimeter mass was felt at the ampulla. Consequently, duodenotomy was done and the small mass appeared grossly to be a benign papilloma. This tumor was excised and immediate frozen section showed it to be a benign papilloma. The ampulla was dilated with Bakes' dilators, the duodenum was closed, and the operation terminated, leaving the anastomosis of the gall bladder to the jejunum. The postoperative course following this operation was completely uneventful and she was discharged from the hospital on the seventeenth postoperative day.

Microscopic diagnosis of this tumor was papilloma of the papilla of Vater.

This patient has been followed by letter 4½ years after operation and has been entirely well until recently when she began having intermittent bouts of a foul-smelling diarrhea. She has had no further symptoms referable to the biliary tract. Approximately 1 year after operation there was one dubious

Fig. 2.

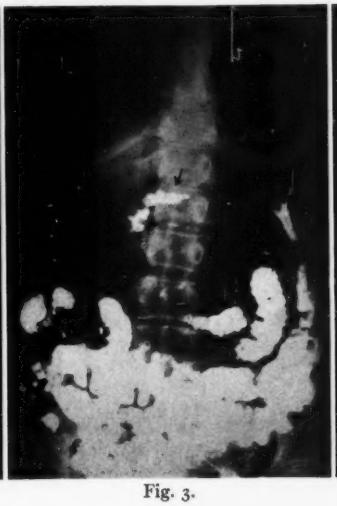

Fig. 3.

Fig. 4.

Fig. 5.

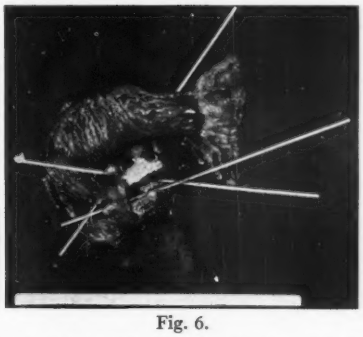

Fig. 6.

Fig. 2. Pancreatic calculi (arrows) confined to the duct of Wirsung in its most distal portion, that is, in the head of the pancreas.

Fig. 3. Pancreatic calculi (arrows) confined to the duct of Wirsung in its most distal portion, that is, in the head of the pancreas.

Fig. 4. Roentgenogram of the specimen resected in Case 3. Several of the calculi were very soft, hence the diffusion of material in this picture of the stones.

Fig. 5. Specimen from Case 3 showing the pylorus, first to third portions of the duodenum and the head of the pancreas which has been incised through the duct of Wirsung to show the cluster of calculi.

Fig. 6. Another view of specimen from Case 3. A probe (*a*) has been passed through the duct of Santorini and emerges through a separate papilla; a second probe (*b*) has been passed through the major pancreatic duct, and the third probe (*c*) through the common duct. The latter two emerge through a common ampulla which is enlarged by carcinoma arising in a papilloma of this structure.

attack of jaundice. There have been no such episodes since that time.

In this patient's history there was evidence that strongly favored common duct stone or malignancy at the ampulla of Vater. Because she was a poor risk, despite the short duration of symptoms, a two stage operation was planned. This small lesion had produced obstructive symptoms with jaundice evidenced by a dilated common duct, without distention of the gall bladder.

The technical details of importance in this case were first, the selection of a two stage procedure because she was a poor risk, and second, the employment of duodenotomy. After adequate mobilization of the duodenum and head of the pancreas to allow accurate palpation of the ampulla, there was reasonable

Fig. 7. Section taken through a papillomatous structure of the ampulla in Case 3. At the inferior margin of the picture is an area of adenocarcinoma (arrow) showing reduplication of the lining of this glandular structure and to the right, two nests of atypical cells with a suggestive alveolar arrangement.

Fig. 8. Malignant adenoma removed in Case 4. This section demonstrates well the benign adenomatous elements at the superior margin of the picture but as one looks inferiorly there is a definite alteration in the orderliness of the pattern with reduplication, hyperchromatosis of the nuclei and invasion of the muscularis.

doubt as to the malignancy of this lesion; hence, duodenotomy was employed with excision and frozen section without completing the resection and thereby sparing this patient a formidable operation for a benign lesion.

CASE 2. This patient was a 33 year old housewife who was first seen at the clinic on September 13, 1948, with the following previous history. In December 1945 the gall bladder was removed because "she had symptoms typical of gall bladder pathology." The roentgenogram had shown a nonfunctioning gall bladder and the gall bladder removed at operation was negative. At this operation a soft rubber catheter was inserted into the cystic duct

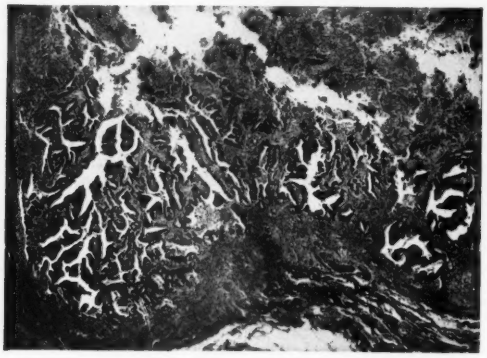

Fig. 9. Papillary carcinoma, removed in Case 5, which arose in a mucosal polyp of the termination of the common duct in the ampulla. The papillary arrangement of this tumor is characteristic.

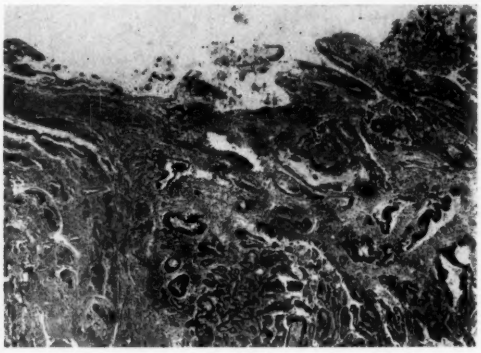

Fig. 10. Photomicrograph of adenocarcinoma, removed in Case 6, which arose in a mucosal polyp of intestinal origin at the ampulla of Vater. In the upper left-hand corner may be seen fragments of the normal duodenal mucosa. Proceeding across the top of the picture are the benign elements of the polyp. The arrows indicate the focus of carcinoma, showing early invasion of the submucosa.

and common bile duct; the catheter came out on her fifth postoperative day. Following discharge from the hospital she had recurrent attacks of pain in the right upper quadrant, not unlike biliary colic, requiring narcotics for its relief. At no time was she jaundiced during any of these attacks. During one of these attacks of pain she was admitted to the hospital. The serum amylase was high and it was thought that she had pancreatitis.

She was readmitted in February 1947, at which time she had a second operation. A markedly dilated common duct containing clear bile and no stones was demonstrated. A catheter could not be inserted into the duodenum and only a fine probe could be passed through the ampulla. This fact was proved by duodenotomy which demonstrated that the tip of the probe definitely was through the ampulla into the duodenum. The surgeon reported that it was not possible to pass a long arm T tube into the duodenum through the pancreatic portion of the common duct. Consequently a T tube was inserted only into the common duct. On the fifth hospital day, "the T tube inserted at operation fell out." Operation was performed for the third time in April 1947 at which time a Roux type of jejunojejunostomy and end-to-side choledochojejunostomy were performed. Postoperatively, a small amount of bile drained which ceased spontaneously. The stools following this operation were positive for bile, the abdomen was negative, and, except for pleuritic pain in the right chest, the remainder of her hospital admission was essentially normal.

Since the last operation this patient continued to have steady right upper quadrant pain, with occasional exacerbations requiring the use of narcotics. The pain remained in the right upper quadrant and extended only partially to the right flank and she had lost approximately 24 pounds during her current illness. Except for tenderness in the right upper quadrant, the physical examination was negative. It was thought that her symptoms could be explained on two possible diagnoses: first, a carcinoma at the ampulla of Vater, and second, fibrosis of the ampulla of Vater. She was admitted to the hospital for the first time under our care October 12, 1948. Urinalysis showed 2 to 5 white blood cells per high power field and 7 to 10 red blood cells per high power field, the hemoglobin was 13.0 grams or 93 per cent, erythrocytes numbered 4,900,000, leucocytes 5,250, the differential smear was essentially normal, cephalin flocculation 0, thymol flocculation 2 plus, thymol turbidity 2.0, and cholesterol 140 milligrams with only a trace of bilirubin in her serum. An intravenous pyelogram was found to be normal. The total proteins were 6.5 and her serum amylase 97 units.

At operation on October 14, 1948, the findings were as follows. After dissection of the adhe ions in the right upper quadrant marked dilatation of the extrabiliary passages was noted measuring up to ¾ of an inch in its greatest diameter. An end-to-side choledochojejunostomy was found partially obstructed both by a narrowed lumen and multiple soft stones. The bile contained much sediment and was green in color. It was impossible to pass a probe into the duodenum through the sphincter of Oddi. The ampulla was visualized through a duodenotomy incision. There was a 4 millimeter projection from the ampulla of Vater into the lumen of the duodenum which had the gross appearance of a papilloma. Frozen section of this tissue was inconclusive except to rule out malignant disease. The extrabiliary passages were intact so far as continuity was concerned. The remainder of the examination was negative. There was no evidence of pancreatitis and no obstruction to the duct of Wirsung. The operative procedure first delineated the choledochojejunostomy, the duodenum was mobilized, transduodenal exploration carried out and the papilloma excised, after which a long arm Cattell T tube was inserted into the common duct, the distal arm passing into the duodenum through the ampulla and split at its proximal portion, with one-half of the tube being inserted to each of the respective hepatic ducts. The choledochojejunostomy was disconnected and the defunctionalized loop of jejunum was resected. A small remnant of cystic duct was found and removed. The postoperative course was uncomplicated. Bile continued to drain through the T tube for 9 days, after which the T tube was clamped. The patient was discharged from the hospital 17 days after the operation.

The microscopic report was benign papilloma of the papilla of Vater (Fig. 1).

The patient has been seen since operation at the clinic. She is asymptomatic and it is planned to remove the T tube at her next visit in February 1949, four months after operation.

The finding of a papilloma of the ampulla of Vater in this patient would answer all of this patient's symptoms prior to and subsequent to her first three operations. It is reasonable to assume that this lesion was present at the previous three operations and that it had produced her symptoms originally. The removal of a nonfunctioning gall bladder without cholelithiasis, with return of symptoms following this procedure, would ordinarily place this patient in the group of patients with "biliary dyskinesia." At the second operation a dilated common bile duct was noted. A probe was passed through the ampulla, but a T tube could not be passed through the duodenum. At her third operation a Roux type of choledochojejunostomy was performed which did not alleviate her symptoms. At the fourth and last operation again a dilated common duct, soft stones obstructing the choledochojejunostomy, fibrosis of the ampulla,

and a definite papilloma of the ampulla of Vater were demonstrated.

Thus, we have demonstrated two excellent causes for this patient's symptoms: first, a benign tumor of the ampulla of Vater, and second, fibrosis of the sphincter of Oddi. It is our opinion that if more attention is paid to the sphincter of Oddi which may become fibrosed, just as fibrosis occurs in the anal sphincter, and if benign lesions are more common than has previously been supposed, and if these lesions are sought, then the diagnosis of "biliary dyskinesia" will be less frequently made and rarely justified.

Technically, this case illustrates again the judicious employment of duodenotomy plus the importance of a long arm T tube described by one of us (4) which is employed in cases that require forceful dilatation or division of the sphincter of Oddi when fibrosis of the sphincter is present.

CASE 3. This 52 year old woman was first seen in the clinic in October 1948 with the following history. For the past 5 years she had had diarrhea with from 3 to 8 bowel movements per day. For the past 6 months she had had constant abdominal pain referred to the back. Until 2 months ago her appetite had been excellent despite the fact that she was constantly, though very slowly, losing weight. In the past 2 months she had anorexia. Her weight for many years was never more than 82 pounds. She had lost 10 pounds in the course of her current illness and at operation weighed 72 pounds. The roentgenograms which she brought with her (Figs. 2 and 3) demonstrated pancreatic calculi which were confined to the head of the pancreas and which appeared to be lined up within the main pancreatic duct. She was admitted to the hospital with a diagnosis of pancreatolithiasis.

Her studies included the following: a hemoglobin of 12.2 grams, erythrocytes 3,420,000, leucocytes 14,450, blood sugar of 79 milligrams per 100 cubic centimeters, chlorides of 98 milliequivalents, bilirubin 0.1 milligram per 100 cubic centimeters, total serum protein 6.4, albumin 3.1, globulin 3.3, and an albumin-globulin ratio of 0.9. The amylase was 109 units. A urine sample taken in the clinic showed 2 per cent sugar despite the normal blood sugar. Preoperatively the diagnosis of diabetes mellitus was not proved but was suspected.

On October 11, 1948, after 3 days of preparation, operation was performed. The findings at operation were as follows: the gall bladder was normal size, the duct of Wirsung was dilated and contained a milky fluid, and the calculi were confined to the duct of Wirsung in the head of the pancreas. In addition, there was an area of low grade pancreatitis in the vicinity of the uncinate process, which had produced a tiny internal pancreatic fistula. Pancreatoduodenectomy was performed in one stage, removing the pylorus, all four portions of the duodenum, the proximal several inches of jejunum, the distal common duct, and the head, neck and uncinate process of the pancreas. During the procedure a rent in the superior mesenteric vein was sutured. The reconstruction was accomplished by an end-to-side pancreatojejunostomy, employing the mucosal suture technique over a rubber tube, an end-to-side choledochojejunostomy, and an end-to-side gastrojejunostomy placed on the efferent or distal loop of the reconstruction. The postoperative course was smooth except for diabetes mellitus of which she had some suggestive evidence before operation. This was treated with diet and insulin. The patient was discharged from the hospital on her sixteenth postoperative day in good condition and taking 15 units of protamine zinc insulin and a 2,200 caloric diet.

The pathologic diagnosis was pancreatic calculi and carcinoma suggesting origin from a papilloma. This tumor surrounded the ampulla and it is difficult to place this lesion either in the ampulla or in the head of the pancreas. Because of its close proximity to the ampulla it has been classified as a carcinoma of the ampulla. Figure 4 is a roentgenogram of the resected specimen. Figures 5 and 6 demonstrate the resected specimen and Figure 7 is a photomicrograph of the tumor.

This patient had two excellent causes for a carcinoma arising in this area. First, she had a long-standing history of inflammatory disease which was confined largely to the head of the pancreas. Second, it can be reasoned that the inflammatory process produced a papillary type of hyperplasia which was followed by malignant degeneration.

The decision to resect this localized accumulation of pancreatic calculi was made because it seemed to offer the best chance for complete relief of symptoms caused by pancreatolithiasis. The carcinoma which was found in this case was discovered by the pathologist in the examination of the specimen after operation.

CASE 4. A 62 year old man was first seen at the clinic on August 21, 1947. His symptoms began 2 months prior to his clinic visit as a dull, steady pain through the right of the upper epigastrium. The pain responded to local heat applications. He felt well until the first week in July 1947 when a generalized itch developed; there was concomitant development of indigestion and gas. He was admitted to a local hospital on August 12, 1947, at which time jaundice was noted for the first time. He had a change in bowel habits from a single daily stool to

3 or 4 light-colored soft stools a day. Prior to these symptoms he had an occasional attack of mild indigestion. He had lost 6 pounds in 2 weeks.

On physical examination he was jaundiced, the liver edge was palpable 3 fingerbreadths below the right costal margin and the gall bladder was not palpable. He was admitted to the hospital on August 22, 1947, with the diagnosis of carcinoma of the ampulla of Vater. The laboratory studies revealed the following: a hemoglobin of 13.4 grams, erythrocytes 4,970,000, leucocytes 8,200, prothrombin time of 110 per cent, nonprotein nitrogen 26, total protein 5.9, cephalin flocculation 0, thymol turbidity 0.2, thymol flocculation 0, colloidal gold 0, urine bile 2 to 5 milligrams, urine urobilinogen 1.5, bilirubin 3.6 milligrams direct, 6.4 milligrams total, total cholesterol 225, alkaline phosphatase 47.2 per cent Bodansky units.

After 3 days of preparation the patient was submitted to operation. The liver was found to be 2 inches below the costal margin. The gall bladder was 8 times normal size, thin-walled, and markedly distended, the common duct was 3 centimeters in diameter, a small, firm nodular lesion about 1 centimeter in diameter was palpated at the ampulla. No gross metastases were demonstrated. Radical pancreatoduodenectomy was performed in one stage, removing the pylorus, all of the duodenum, several inches of the proximal jejunum, the head, neck, and uncinate process of the pancreas and lower common bile duct. The jejunum was closed and the reconstruction was as follows: the stomach was anastomosed to the jejunum, end-to-side, on the afferent loop. The next anastomosis was an enteroenterostomy, defunctionalizing a 12 inch loop of jejunum, and onto this loop was implanted the pancreas and the common duct.

The patient's postoperative course was complicated by a moderate degree of obstruction of the gastrojejunostomy which responded to conservative treatment (Levin tube). He was discharged from the hospital on the thirty-second postoperative day.

The pathologic report was malignant adenoma of the ampulla of Vater and fibrosis of the pancreas (Fig. 8). This patient was seen at the clinic in October 1948 and is well, without symptoms, 14 months after resection.

In 1941 Horsley reported a one stage pancreatoduodenal resection for a lesion which was thought to be carcinoma at operation. The microscopic report on the tumor was benign adenoma of the ampulla which had produced signs and symptoms of malignancy. Similarly, Christopher reported a case of benign adenoma of the ampulla in a review of the literature on the subject in 1933. This case, presented here, is an example of malignancy occurring in an adenoma that had produced symptoms of 2 months' duration, with the first symptoms being pain which was followed later by jaundice.

CASE 5. A 55 year old man was first seen in the clinic on December 20, 1948, with jaundice as his chief complaint. He noted dark urine and clay-colored stools with the onset of the jaundice, but the stools had gradually become colored again. He had lost 10 to 15 pounds in the past 5 weeks during which time he had had painless jaundice. There was no history of recent blood or plasma transfusion. He was thoroughly studied at another hospital. The gall bladder was not visualized; the gastrointestinal series and barium enema were negative.

On physical examination the patient was deeply jaundiced; the liver edge was palpable and the gall bladder could not be palpated.

On admission to the hospital the hemoglobin was 11.4, erythrocytes numbered 4,390,000, leucocytes 13,800, prothrombin time was 104 per cent and blood sugar 83 milligrams, nonprotein nitrogen 28 milligrams, total protein 5.6 and 1.1 albumin-globulin ratio, bilirubin 12, cholesterol of 172, chlorides of 495 milligrams per 100 cubic centimeters. He was submitted to surgery after a week of preparation and at operation a markedly distended gall bladder and dilated common duct were noted, the pancreas was completely negative to palpation, the duodenum and the pancreas were mobilized and only after this maneuver was accomplished was it possible to feel a small polypoid lesion at the ampulla through the duodenum. The duodenum was opened because it was thought that this might possibly be a benign lesion. Papillomatous material was expressed from the enlarged ampulla and on frozen section this material was reported as a papillary type of carcinoma of low grade malignancy. Consequently, the duodenum was closed and a radical pancreatoduodenectomy in one stage was accomplished successfully. The pylorus, all of the duodenum, the proximal 6 inches of jejunum, the head, neck, and uncinate process of the pancreas and the lower common duct were resected. The reconstruction was accomplished by anastomosing the end of the stomach into the end of the jejunum, an enteroenterostomy was made between the afferent and efferent loops of the jejunum, and the pancreas and common duct were reimplanted into the defunctionalized loop of jejunum. All of these anastomoses were in an antecolic position. This patient withstood the operative procedure well and he is currently in the hospital making a satisfactory recovery after a secondary operation for the removal of the spleen for an intractable toxic thrombocytopenic purpura.

The final microscopic report was malignant adenoma of the ampulla arising in a mucosal polyp of the terminal common duct (Fig. 9).

At operation this patient had the classical findings associated with carcinoma of the ampulla of Vater. The gall bladder was greatly distended, and the common duct was dilated,

yet the lesion was not palpable until the duodenum and the head of the pancreas were adequately mobilized. Following this maneuver the lesion was palpated through the duodenum as a pedunculated tumor. Despite the fact that all the evidence pointed toward malignant disease, duodenotomy was done with frozen section to prove this a malignant tumor.

CASE 6. This 70 year old woman was first seen at the clinic on October 28, 1948, with the chief complaint of dull ache in the epigastrium and back of 10 years' duration. The pain in the epigastrium had been intermittent and had extended through to the back and she had occasionally felt the pain in the right upper quadrant. During these attacks her appetite had been poor but the pain had not been affected by changing to a bland diet. She had a definite selective food dyspepsia and on occasion nausea and vomiting had accompanied the pain. Since February 1948 she had had 3 episodes of steady pain; the last occurred 3 weeks prior to her visit to the clinic and lasted for 3 weeks. During the last 10 years she had had continuous upper abdominal gas with belching, shifting gas pains, and the passage of great amounts of flatus. Six years ago she was told that she had sugar in her urine; however she had never taken insulin, and she had had no weight loss.

On physical examination the patient was well developed, obese, elderly, and not acutely ill and, except for a questionable mass in the left upper quadrant, the physical examination gave negative results. The studies at the clinic included an oral cholecystogram by which the gall bladder was not definitely visualized, a barium enema which showed spasticity of the sigmoid and descending colon, and an upper gastrointestinal series which was normal, no defects being observed either in the stomach or duodenum. She was treated for a degenerative arthritis, for spondylolisthesis and for obesity. She was fairly well until Christmas of 1948 when she had a shaking chill, followed by fever. The following day the urine became dark, the stool light and the sclerae yellow. During this episode of chills and fever she had a severe pain in the midepigastrium which extended through to the midback, accompanied by nausea, and she vomited a small amount of bile. The jaundice lasted for about 1 week and then gradually all external signs disappeared. From this history a diagnosis of common duct stone was made and she was admitted to the hospital on January 24, 1949.

On admission to the hospital the hemoglobin was 15.5 grams, erythrocyte count 5,020,000, leucocyte count 7,500, with a normal differential. The prothrombin time was 6 minutes, or 100 per cent of normal. There was only a trace of bilirubin in her serum. The blood sugar was 117 milligrams per 100 cubic centimeters. After 2 days of preparation she was submitted to surgery on January 26, 1949.

When the peritoneal cavity was opened the liver appeared to be normal, and the gall bladder was distended with bile but contained no stones. It was normal in size. Its walls were thickened and edematous. The common bile duct and common hepatic duct were greatly dilated, being ¾ inch (1.9 cm.) in diameter. When the common hepatic duct was opened, no stones were found; however, neoplastic tissue was obtained with a stone forceps from the region of the ampulla of Vater. Frozen section of the tissue was obtained; however, it was difficult to make a diagnosis of malignant disease from this specimen. Consequently, a T tube was sutured into the common hepatic duct and duodenotomy was performed. The ampulla was visualized and it appeared grossly to be involved by a tumor. The tumor was confined to the lumen of the ampulla without evidence of extension onto the duodenum. A positive diagnosis of malignancy was made from specimens obtained by this approach. The remainder of the exploration was negative. There were no lymph nodes in the gastrohepatic omentum or ligament of Treitz.

With the diagnosis established, the duodenotomy incision was closed and a radical pancreatoduodenectomy performed, removing the pylorus, most of the duodenum, the head and neck as well as the uncinate process of the pancreas, and the distal portion of the common duct. The distal end of the fourth portion of the duodenum was closed and passed behind the ligament of Treitz into the general peritoneal cavity. This was followed by an end-to-side pancreatojejunostomy with mucosal anastomosis of the duct to the mucosa of the jejunum and buttressing the rest of the pancreas to the incised serosa of the jejunum. A short section of rubber tubing was used in this anastomosis.

Distal to this anastomosis the end of the common duct was anastomosed into the side of the jejunum and distal to this anastomosis an end-to-side gastrojejunostomy was performed. It will be noted that the gall bladder was removed initially during this operation. She was discharged from the hospital in good condition on February 17, 1949.

The microscopic permanent sections of this tumor showed it to be an adenocarcinoma arising in a mucosal polyp which itself arose from intestinal epithelium adjacent to the lining of the ampulla of Vater. The gall bladder was diagnosed as chronic cholecystitis. The appendix which was removed was negative.

In reviewing this patient's history, with the diagnosis established by operation, it becomes apparent that she had at least a 10 year history of biliary colic with associated symptoms which pointed to the extrahepatic biliary tract. The symptoms were progressively severe until her initial visit to the clinic in October 1948. At that time a complete gastrointestinal study

revealed a single positive finding, that is, a gall bladder which was not visualized. Up to this point in her history in retrospect it must be assumed that her symptoms were being produced by a polyp situated in the ampulla, which was benign. Some degree of obstruction of the common duct must have existed for some time but was insufficient to produce jaundice. In the 2 month interval, or perhaps over an even longer period, the mucosal polyp of the ampulla increased in size, obviously by the occurrence of malignant degeneration, and transiently obstructed the common duct, producing externally visible jaundice for the first time on December 25, 1948. The jaundice disappeared prior to surgery.

This case serves to add emphasis to the remarks previously made. This patient's gall bladder was distended with bile and upon removal, contained no stones. The common duct was enlarged and upon exploring it, no stones were found but tumor tissue was obtained with a stone forceps from the region of the ampulla of Vater, from which a diagnosis of malignancy could not be made. Consequently, duodenotomy was performed, the ampulla visualized, a positive diagnosis of malignancy was made from the frozen section, and radical resection carried out successfully.

In a discussion of this case with Dr. W. A. Meissner, the pathologist, he remarked that this tumor had an appearance similar to that seen so frequently with polyps of the rectum which have undergone malignant degeneration. Thus, our assumption that these lesions, originally benign, have undergone malignant degeneration is well illustrated by this patient's history, the operative findings, the resected tumor, and finally the photomicrograph (Fig. 10).

DISCUSSION

Since we have discussed each case separately, we need only to point out that their presentation is evidence to support the views expressed by Baggenstoss.

The 2 cases of benign papilloma produced symptoms and objective signs of obstruction of the common duct. The 4 cases of malignant lesions which were presented emphasize the importance of the premalignant status of these benign lesions. Malignancy of the ampulla which frequently arises in such lesions is usually of a low grade character, metastasizes late, gives early symptoms which lead to early diagnosis and treatment by radical pancreatoduodenectomy. We (5) have recently reported an experience with 57 resections for malignant disease of the ampulla, head, lower common duct, and duodenum, and the ampullary lesions were shown to be the most favorable with respect to survival, cure, and palliation. Of 12 patients whose course was followed for 5 years or longer, 6 or 50 per cent who had carcinoma of the ampulla and resection lived 3 years or over and 3 patients, or 25 per cent of this group, are still alive and well 5 years or more since operation.

In an excellent review of carcinoma involving the peripapillary portion of the duodenum by Lieber, Stewart, and Lund in 1939, these authors called attention to the fact that in 25 instances carcinoma of the ampulla went unrecognized at operation, and that a correct diagnosis was made by celiotomy in 68 per cent of 122 cases.

We believe that in most instances, carcinoma of the ampulla and head of the pancreas can be diagnosed accurately at operation by observing the dilatation of the extrahepatic biliary tree, by dilatation of the duct of Wirsung, and by mobilization of the duodenum and head of the pancreas for accurate palpation of the ampulla and head of the pancreas. One is hesitant, however, to do a formidable procedure such as pancreatoduodenectomy if the above criteria are not present. When reasonable doubt exists about the malignant nature of the lesion, it is recommended that duodenotomy with biopsy and frozen section be done as was demonstrated by Cases 1, 2, 5, and 6. If the lesion is benign, local excision will obviously be sufficient. If the lesion proves to be malignant, then radical pancreatoduodenectomy must be done if one expects to cure or materially prolong life in carcinoma of the ampulla.

SUMMARY

We have presented 2 cases of benign papilloma of the ampulla and 4 cases of malignancy of the ampulla which apparently arose from

premalignant lesions, such as papilloma, polyp, or adenoma. These benign lesions are *relatively* common and are important in the production of symptoms as well as being a source of malignant disease. We wish to suggest these benign lesions as a possibility in patients who have had cholecystectomy with recurrence of symptoms. These lesions are small and in most instances, if symptomatic, such lesions will continue to be diagnosed at operation by mobilization of the duodenum and head of the pancreas for accurate palpation and by duodenotomy with direct visualization of the ampulla of Vater. When these lesions are asymptomatic, they will probably continue to be incidental findings at autopsy.

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THE ANATOMY OF THE HERNIAL REGIONS

III. Obturator Hernia and General Considerations

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IN a relatively restricted zone in the abdominopelvic wall, four areas of potential herniation occur. The upper two are inguinal (indirect and direct); the intermediate is femoral; the lower is obturator. They follow an almost vertical line approximately two inches in height. The site of protrusion for indirect inguinal hernia is located to the lateral aspect of the inferior epigastric vessels; the point of femoral protrusion is the canalicular space situated lateral to the lacunar prolongation of the inguinal ligament. The anatomy of these hernial areas has been reviewed in the two preceding articles.

The site of obturator herniation is the pelvic orifice of a tubular canal through the anterosuperior portion of the obturator membrane. The form and relations of the canal will be described and figured, and, in conclusion, the three areas will be compared in respect to strength against herniation.[1] The discussion hereinafter presented deals not with a true peritoneal sac with enclosed viscera, but with a lipomatous protrusion of the preperitoneal layer into the obturator canal. In approximately 360 body-halves the authors and their colleagues found no case of serous hernia into the obturator canal, and only 6 instances of preperitoneal protrusion. In a smaller series of 166 (including some of the preceding lot of specimens) there were 27 cases of indirect inguinal hernia. In 230 body-halves 10 cases of femoral hernia were encountered; only one of these was serous, the others being examples of hernia adiposa.[2]

Contribution No. 505 from the Department of Anatomy, Northwestern University Medical School.

[1]Based upon special study of selected specimens in the total series of 250 (500 body-halves), the several types of hernia and related anatomical features have been discussed in illustrated articles, by the senior author and his assistants, published in the following issues of the *Quarterly Bulletin of Northwestern University Medical School:* 1941, vol. 15: 32-38 (inguinal coverings of the round ligament of the uterus); vol. 15: pp. 114–121 (indirect inguinal hernia); vol. 15: 192–204 (direct inguinal hernia); 1942, vol. 16: 128–141 (indirect inguinal hernia); vol. 16: 203–208 (obturator hernia); 1943, vol. 17: 36–49 (femoral hernia).

MATERIAL AND METHODS

An adult male specimen was the subject of study. A complete set of dissections was carried out, from peritoneum to parietal musculature and from fascia lata to the obturator membrane. A drawing was made for each of the major levels in the dissection (Figs. 1 to 5).

OBSERVATIONS AND DISCUSSION

1. *Peritoneum.* In the anterior portion of the lesser pelvis, with which region the present account is concerned, the peritoneum covers the superior surface of the urinary bladder, to be reflected upward therefrom to the greater pelvis and the abdominal wall. Neither the outlines of the bladder nor margins of the external iliac vessels are clearly definable beneath the intact peritoneum. The form of each is masked by the preperitoneal tissue which envelops all pelvic viscera and associated blood vessels. In the present consideration the existence of such a sheath is particularly important, since it not only behaves as a cushion guarding the obturator canal against diverticular herniation of the overlying peritoneum, but also (as in the case described hereinafter) may be the source of a fatty process, which, in the form of a hernia adiposa, comes to occupy the obturator canal.

2. *Preperitoneal tissue.* The preperitoneal tissue in which the pelvic organs and vessels are housed, fused with the visceral portion of the endopelvic fascia, is carried upward to the inguinal wall, into the iliac fossae, and over

[2]According to Watson (*Hernia*, 2nd ed., 1910), inguinal hernias constitute 92 per cent of all hernias (indirect type making up 84 per cent of all inguinal hernias in the male). Femoral hernias constitute 2.5 per cent of all hernias (97 per cent of them occurring in females). Assumedly because the obturator type is excessively rare, statistical occurrence is not recorded.

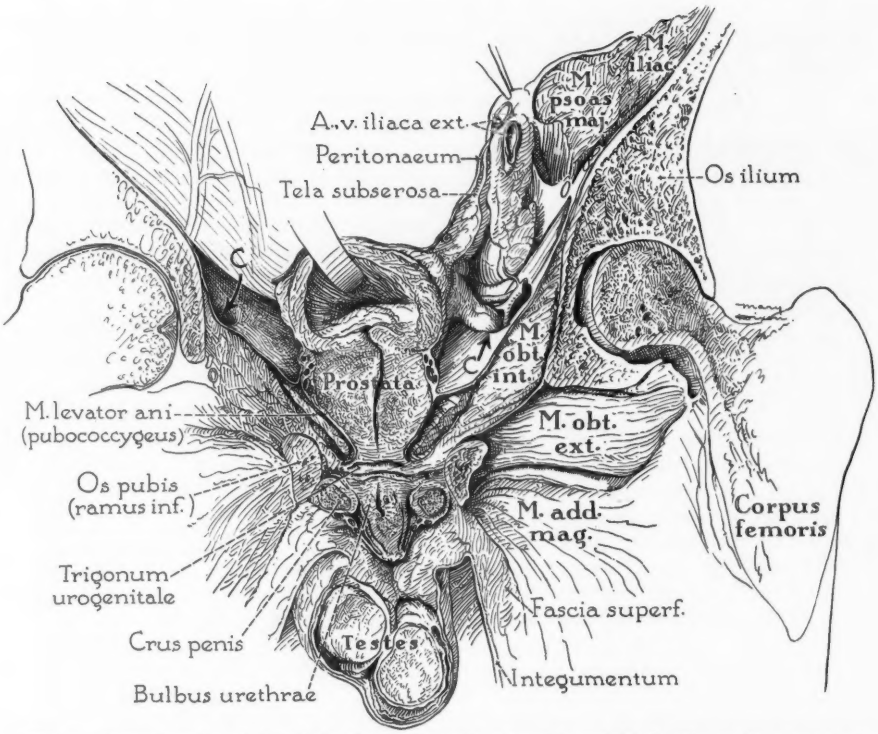

Fig. 1. Coronal section of the pelvis of an adult male, viewed from behind. The section passes posterior to the obturator canals and cuts through the following structures: the pubococcygeal portion of the levator ani; the sphincteric musculature and fasciae of the deep perineal compartment; the cavernous bodies and muscles in the superficial perineal compartment; the scrotum and testes; the adductor and obturator muscles of the proximal part of the thigh. The peritoneum and the preperitoneal tissue have been elevated on the right side to demonstrate the obturator hernia (at arrow *C*). These layers have been removed on the left (empty obturator canal indicated by arrow *C*). The heavy preperitoneal layer is chiefly fatty; it is relatively thin in the greater pelvis, but thick in the lesser pelvis where it passes between the external iliac vessels and the urinary bladder.

the vertebral column as a definite sheet which thins as it ascends (Fig. 1). In the area with which the present account is concerned, the layer is disposed in the form of a wing-like prolongation of the fibrous envelope of the bladder; in both the greater and lesser pelvis this is readily removable by blunt dissection from the subjacent superior fascia of the pelvic diaphragm and the fascial covering of the obturator internus muscle (Fig. 1, right side). The layer contains an appreciable fatty deposit, and it is moderately thick as it overlies the orifice of the obturator canal.

3. *Endopelvic fascia.* The parietal portion of the endopelvic fascia, against which the preperitoneal layer rests, constitutes the covering of the obturator internus muscle (Figs. 1 and 2). At the margin of the obturator canal it is carried into the latter Figs. 1 and 2, at arrows *C*); it fuses with the tissue of the obturator membrane and with that of the surrounding periosteum. Externally it appears deep to femoral muscles which arise from the body and rami of the pubis (Fig. 5, at ✠).

4. *Obturator membrane and musculature.* The obturator membrane, it will be recalled, is a strong fibrous sheet which almost completely closes the obturator foramen in the innominate bone. Owing to the fact that both the obturator internus and obturator externus

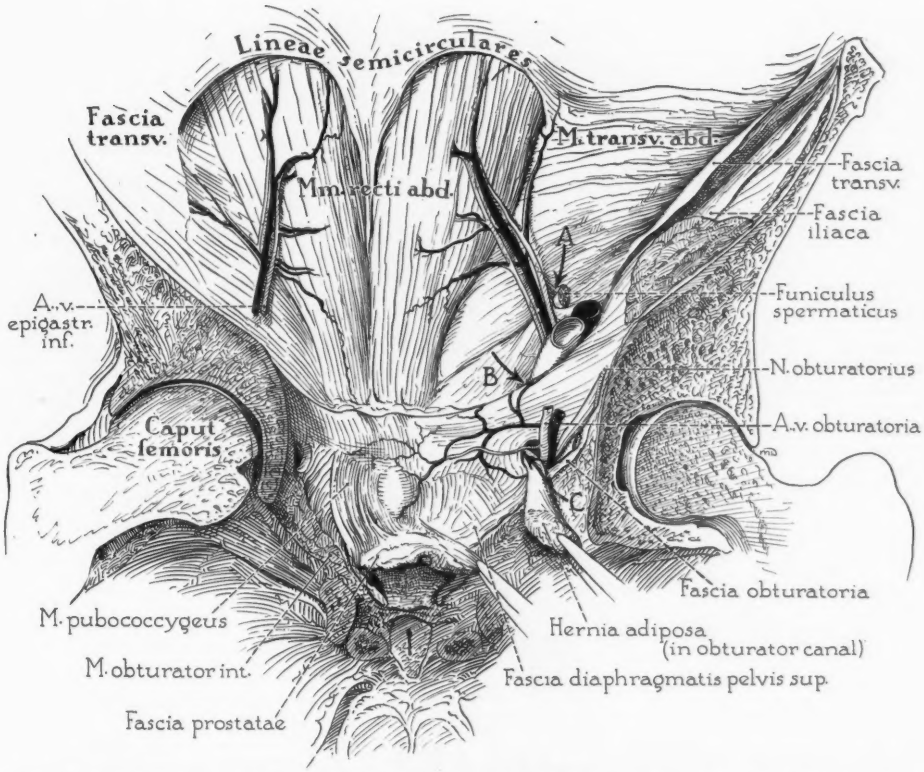

Fig. 2. Same specimen, deeper dissection. The peritoneum and the preperitoneal tissue have been removed. The hernia adiposa is a finger-like process of the subserous tissue; it has been transected and pulled downward. On the left side, the investing fascia has been removed from the levator ani and from the muscles of the anterior abdominal wall. On the right side the obturator vessels have been mobilized, the structures of the spermatic cord cut at the abdominal inguinal ring, and iliac vessels transected near the point where they pass beneath the inguinal ligament. The three hernial areas are thus exposed, and their general relations shown: the inguinal (at arrow *A*) in the musculofascial wall of the lower abdomen; the femoral (arrow *B*) bounded by ligaments, bone and blood vessels; the obturator (arrow *C*), a hiatus in a ligament which is strongly buttressed by obturator muscles on both the inner (pelvic) and outer (femoral) aspects.

muscles take partial origin from this membrane, it is actually aponeurotic, not "membranous" in nature. The fault in the membrane is situated in its anterosuperior portion, just beneath the shelving obturator crest on the pelvic aspect of the superior pubic ramus. The crest is the roof of a groove; the groove is converted into a canal by the membrane. Through this obturator canal vessels and nerves of the same name pass from the pelvis to the medial aspect of the thigh.

Obviously, an adjacent part of the preperitoneal layer could be pressed through the pelvic orifice of the canal, to share the space of the latter with the obturator artery, vein, and nerve. In the present case such a pedunculated mass extends from the obturator or internal aspect of the preperitoneal layer into the obturator canal inferior to the obturator vessels and nerve (Figs. 1 and 2, arrows *C*). Despite this displacement of the retroperitoneal stratum, the peritoneal layer in the region of the obturator canal is smooth; it is not foveate toward the orifice of the canal.

The sharply defined margins of the inner aperture of the obturator canal become evi-

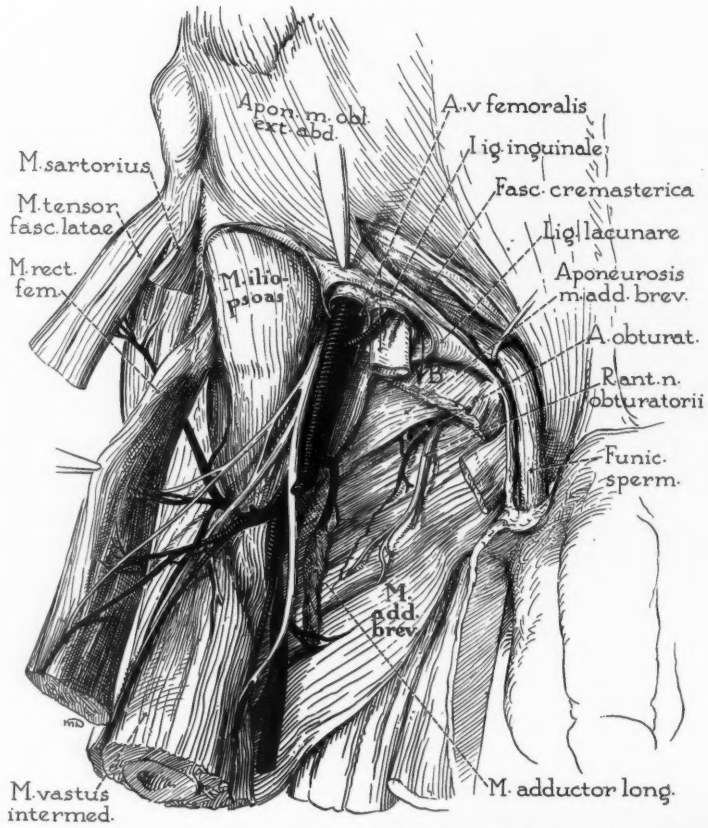

Fig. 3. Same specimen, viewed from the front. In the inguinal region the external oblique aponeurosis has been reflected along the line of the subcutaneous inguinal ring. When the crura have thus been turned aside, the internal oblique layer and its cremasteric prolongation upon the spermatic cord are exposed. The inguinal ligament has been freed from the fascia lata; the latter has been removed distally, its margin lifted to reveal the structures in the proximal part of the thigh (especially those of the femoral triangle). In lifting the ligament, the iliopsoas muscle is shown laterally in the muscular lacuna; also exposed are the femoral vessels and the femoral canal (arrow *B*) of the vascular lacuna, and the lacunar ligament which bounds the femoral canal medially. Laterally, the tensor fasciae latae, the sartorius, and the rectus femoris muscles have been cut and turned aside to show the muscular rami of the arteries and nerves; the iliopsoas muscle lies *in situ*. The femoral artery has been transected just distal to the point of origin of the deep femoral branch; the femoral vein has been cut near the inguinal ligament, all of its tributaries excised. Medial to the femur, the pectineus muscle remains only at the extremities (cf. Fig. 4); the adductor longus muscle has been cut. By removal of these structures of the obturator area, the aponeurotic edge of the adductor brevis is shown; the aponeurosis overhangs the superior margin of the obturator canal. Beneath this edge the obturator artery and the anterior branch of the obturator nerve emerge, to descend upon the adductor brevis muscle (the latter is intact behind the transected adductor longus muscle).

dent when the peritoneal layer and the underlying preperitoneal tissues are removed (Fig. 2). The internal, or pelvic, aperture of the canal, is oval, with the long axis in the vertical plane. Approximately two-thirds of the circumference of the orifice is composed of bony wall, while the remainder is formed by the sharp margin of the strong obturator membrane. Superiorly, laterally, and inferolaterally the bony limits of the inner orifice are the walls of the obturator on the inferior aspect of the superior ramus of the pubic bone. Medially and inferomedially the margin of the aperture is the assemblage of muscular and

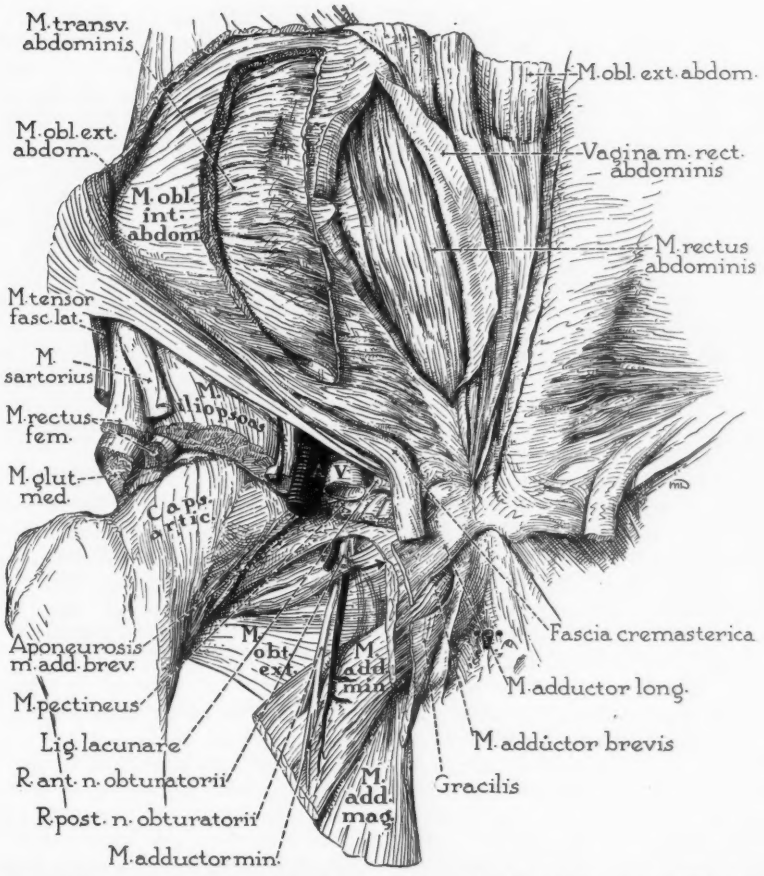

Fig. 4. Same specimen, deeper level. The external oblique has been completely turned aside (medially to the opposite side and laterally over the anterior iliac spine). A window has been cut in the internal oblique to reveal the subjacent transverse abdominal muscle, down to the point at which the fleshy part becomes continuous with the fascial portion of the same layer. The rectus sheath has been opened by a longitudinal cut, the aponeuroses retracted to show the contained muscle. In the thigh the following muscles have been cut close to their origins: tensor fasciae latae, sartorius, rectus femoris (both heads), iliopsoas, pectineus. Also transected, but remaining as longer portions, are the following muscles: adductor longus, adductor brevis, adductor magnus. The obturator externus is intact. The anterior division of the obturator nerve has been cut near the point of emergence from the foramen; the posterior division remains intact. The femur and the capsule of the hip joint are exposed. In the perineum the external genitalia have been removed. The adductor brevis has been cut in such a way as to demonstrate that it arises not only from the inferior pubic ramus, but also from the superior ramus (above and lateral to the arrow) and the capsular tissue of the hip joint. Before removal of the muscle, the capsular tissue was continuous with the aponeurosis of the adductor brevis.

membranous structures mentioned before. The vertical diameter of the pelvic orifice is 1.8 centimeters; the transverse diameter is 1.3 centimeters. The orifice leads into the obturator canal, a cylindrical passageway 2 centimeters in length.

5. *Medial femoral musculature.* Whereas, the canal through which a femoral hernia reaches superficial level in the thigh rests upon the free surface of the pectineus muscle-fascia, the small channel through which an obturator hernia gains exit from the pelvis lies

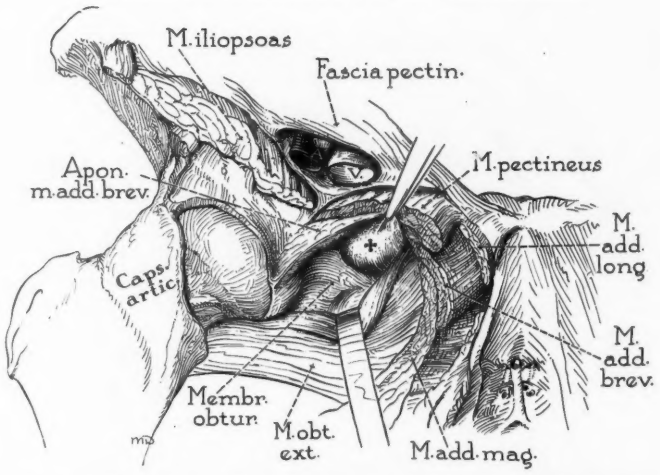

Fig. 5. Same specimen. Dissection carried to the level of the obturator membrane and obturator canal. The capsule of the hip joint has been partly removed to show the relation between the obturator structures and the head of the femur. The pectineus and the adductor longus have been cut close to their origins. The adductor brevis muscle and its aponeurosis have been retracted cranialward with the underlying hernial protrusion (at ✣). The obturator externus has been freed from the obturator membrane, and retracted caudalward. It is thereby demonstrated that the origin of the adductor brevis extends lateralward to fuse with the capsule of the hip joint, and that, in being thus prolonged, it normally covers the external aperture of the obturator canal (latter here occupied by a hernial mass).

beneath not only the pectineus itself, but also under two neighboring muscles, namely, the adductor brevis and the obturator externus. Moreover, the muscles are even more strongly held in their positions over the obturator canal by the adjacent adductor longus and adductor minimus, and by a pubic wing of attachment of the articular capsule of the hip joint (Figs. 3 to 5). These muscular and ligamentous barricades will be considered in the order of succession from deep to superficial level.

The adductor brevis muscle is most intimately associated with the external orifice of the obturator canal. It is conventionally described as arising by a narrow origin from the outer surface of the inferior ramus of the pubis. Actually, its area of origin is far more extensive. The fleshy part does arise as regularly described (in Fig. 4, upward to the arrow). However, additionally, the origin is carried lateralward to the femur (lateralward, beyond the arrow in Fig. 4). This aponeurosis of origin is strong and wide (Fig. 5) and is part of the capsule of the hip joint (Figs. 4 and 5); it merges with the fascial sheath of the overlying pectineus muscle.

Only the superior margin of the obturator externus muscle is related to the obturator orifice (Figs. 4 and 5). The muscle arises from the rami of the pubis, the inferior ramus of the ischium, and from the outer surface of the obturator membrane. In the obturator region, as a flat, strong plate, the obturator externus muscle lies deep to the aponeurosis of origin of the adductor brevis (Figs. 3 and 4).

The pectineus lies superficial to the above-described muscles (Figs. 3 to 5). It arises from the pectineal line on the superior ramus of the pubis, from the surface of the pubis in front of that line, between the iliopectineal eminence and the pubic tubercle. Additionally, it is attached through its own fascia, to the subjacent aponeurotic origin of the adductor brevis (Figs. 3 to 5).

The adductor longus muscle lies in the same plane as the pectineus, covering the adductor brevis (Figs. 3 and 4). In arising from the area of the symphysis of the pubis, and in coursing

obliquely downward and lateralward to the linea aspera of the femur, it covers part of the adductor brevis.

These muscles are so closely applied to one another that the obturator vessels and nerves are allowed no distinct hiatuses of emergence. The anterior division of the obturator nerve pierces the anterior part of the fascia covering the external opening, and courses between the two layers that form the adductor brevis aponeurosis; the posterior division of the obturator nerve descends on the posterior surface of the pubic head of the obturator externus muscle; it then pierces the fascia between the pubic and ischial heads, and finally lies on the anterior surface of the ischial head of the obturator externus.

CONCLUSIONS

Medial femoral and parietal pelvic muscles, together with strong ligaments, guard the osseomembranous obturator canal. The canal, itself oblique, ends externally at the superior border of the thick obturator externus muscle. The upper border of the latter muscle occupies an oblique sulcus. The sulcus is produced by the aponeurosis of the adductor brevis. The aponeurosis is attached to the outer crest of the obturator canal and extends laterally to the capsule of the hip joint. The canal is small, transmitting lesser nerves and vessels; it constitutes a minor fault in the pelvic portion of the abdominopelvic space. Internally the small orifice is buffered by a strong, relatively thick wing of locally thickened preperitoneal connective tissue, and narrowed by the obturator internus muscle. Externally the orifice is equally small; it is not merely bordered by muscles, but completely covered by them.

Turning now from the anatomy of the obturator region in particular to a general comparison of the three hernial areas, it may be said that in the femoral region the structures which surround the femoral ring and canal do not constitute as effective a barricade against herniation as do the boundaries of the obturator canal. In the former region, the continuations of the external iliac vessels enter the femoral triangle at the approximate middle of the line of fusion of pelvic and abdominal layers. Descending upon them in front is the innermost one of the three anterolateral abdominal layers, viz., the transversus abdominis; behind lies fascial investment (actually of aponeurotic nature) of the iliopsoas muscle. Converging upon the vessels, these conjoined fasciae form an outer femoral sheath. Within this coat lies the immediate packing for the vessels, the preperitoneal connective tissue, which is prolonged upon the artery and vein into the thigh, as an internal sheath. The "space" within the sheath is filled in approximately the lateral two-thirds by the femoral vessels, but is empty (save for areolar tissue and lymphatic elements) in its medial one-third; the latter "space" is the femoral canal. The peritoneum rests almost directly against the internal orifice (femoral ring) of the canal; only the thin preperitoneal layer intervenes. The latter relationship makes for weakness against herniation; however, strength is lent circumferentially by other anatomic structures, namely, a strong ligament (lacunar) medially, a taut ligament (inguinal) superiorly, a bone (pubis) inferiorly, and of vessels (femoral) laterally.

Of the three sites on the inguinopelvic wall at which herniation may occur, the inguinal is least resistant. In descent of an indirect hernia a funicular process is merely made more capacious, displacement of investing coats being possible on three of the four aspects. In succession, the abdominal orifice (or ring) is dilated, the inguinal opening is distended, and the space bounded by the crura at the subcutaneous ring is widened. Once the peritoneal diverticulum is occupied, further extension is not hindered by the presence of strongly resisting structures. When the hernia has reached a point midway between the rings, the overlying external oblique is represented by fascia bridging the gaps between the aponeurotic crura; crura are displaceable and the fascia is extensible. Progress of the hernia, therefore, becomes easier as the mass advances toward the subcutaneous level. The investing internal oblique (cremaster layer) is regularly fascial and, therefore, is merely a thin, weak, intermediate covering. The funicular derivative of the transverse abdominal muscle is almost without exception purely fascial—usually so thin that the underlying fatty

lobules in the preperitoneal layer can be seen clearly through it. Altogether, then, the layers form lamellae of a five-layered tube, through the innermost of which the hernial mass advances, expanding in succession, a serous layer (the processus vaginalis), a thin, areolar stratum, and three layers which are principally fascial in structure and which are locally anchored to bone only on the inferior aspect.

In summarizing, then, it may be said that the fascial lining of the abdominopelvic cavity extends outward, as normal tubes, at three points: anteriorly into the thigh as the femoral sheath; in the groin as the internal spermatic (infundibuliform) fascia; to the medial musculature of the thigh as the lining of the obturator canal. The inguinal canal contains the ducts of the testis with associated small visceral vessels and nerves, or, in the female, the round ligament of the uterus; the femoral transmits a pair of large vessels; the obturator carries small vessels and nerves, destined to supply musculature chiefly in the immediate area, viz., the proximal part of the adductor region. The preperitoneal tissue of the inguinal canal is areolar and fatty. Of the three, the inguinal is least well guarded by musculature and skeletal structure; the obturator is most effectively barricaded.

Upon the basis of anatomical structure it would be expected that herniation would occur in the following order of frequency; inguinal, femoral, and obturator—an order actually obtaining, as evidenced by laboratory and clinical experience.

THE EFFECTS OF INJECTION OF PENICILLIN, PEANUT OIL AND BEESWAX, SEPARATELY AND IN COMBINATION, UPON NERVE AND MUSCLE

An Experimental Study

THOMAS J. HOLBROOK, M.D., and COBB PILCHER, M.D., F.A.C.S., Nashville, Tennessee

SINCE penicillin was first introduced into clinical medicine, various methods have been utilized in an attempt to reduce the frequency of injections necessary to maintain adequate therapeutic blood levels. In 1944, Romansky and Rittman (3, 4) used a mixture of penicillin, peanut oil, and beeswax in order to delay the absorption of penicillin from the tissues. A suspension of penicillin in peanut oil and beeswax was later developed for commercial use and consisted of 4.8 per cent U.S.P. white beeswax in peanut oil with 300,000 units of either the calcium or sodium salt of penicillin.

In the clinical use of this material different types of undesirable reactions have been observed (1, 2, 5). In addition to general reactions, presumably allergic in nature, local phenomena have been noted at the site of injection. Among these have been pain, tenderness, induration, sterile abscess formation, and the development of "tender nodules."

Romansky (2) has studied the changes produced in muscle after the injection of calcium penicillin, peanut oil, and beeswax. In specimens obtained from patients who had expired 1 to 2 months after they had received numerous intramuscular injections, he found only a few giant cells and minute cysts with thin fibrous walls. In hamsters and rabbits followed 3 to 6 months after the intramuscular injection of this material, Romansky found essentially the same changes. He found no evidence of muscle necrosis and very little fibroblastic reaction. In the lungs of rabbits, followed at intervals up to 72 hours after the intravenous injection of penicillin in peanut oil and beeswax, Bondy, Sheldon, and Weems found a granulomatous process and thrombosis of small pulmonary arteries. In this same study of beeswax (4.8 per cent white wax U.S.P.) in peanut oil and peanut oil alone, they obtained evidence which suggested that the severity of the inflammatory reaction was due to the irritative effect of the wax. That even more serious consequences might sometimes attend the injection of penicillin in oil and wax, was forcibly illustrated by the following case, observation of which led to the experimental study to be reported herein.

REPORT OF CASE

R.C., V.U.H. No. 165029, male, aged 30 years, received an injection of 300,000 units of calcium penicillin in 1 cubic centimeter of peanut oil and beeswax into the middle third of the posterolateral aspect of the left arm 1 month before he was referred to the neurosurgical service by his family physician. As the injection was begun, he experienced pain and numbness in his hand and the extended hand fell into a position of flexion at the wrist. Evidence of complete radial nerve paralysis was present at the time of his admission, a month later.

At operation, the radial nerve was found to be completely necrotic for a distance of 10 centimeters with disruption of its continuity. The muscle adjacent to the nerve was also necrotic.

METHOD

Twenty-seven dogs, weighing from 3.7 to 8.8 kilograms, were used in these experiments. The animals were anesthetized with sodium pentobarbital given intravenously. With aseptic technique, the sciatic nerve in the

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Dr. Holbrook was William Henry Howe Fellow in Neurosurgery, 1947 to 1948.
Dr. Pilcher died since the preparation of this article.
This study was aided by the John B. Howe and Jack Fies Funds for Research in Neurosurgery.

TABLE I.—INTRANEURAL INJECTION

Type of material	Isotonic NaCl	Calcium penicillin, oil and wax	Peanut oil	Beeswax and peanut oil	Calcium penicillin	Sodium penicillin
No. experiments	11	12	6	11	5	5
Duration, days	7–36	2–36	5–42	2–58	2–58	9–28
Persistent paralysis of nerve Complete	0	10	0	0	4	2
Partial	0	2	0	7	1	1
Macroscopic changes Normal	11	0	4	0	0	2
Necrosis and exudate	0	7	0	0	1	0
Enlargement and adhesions	0	12	2	11	5	3
Microscopic changes Normal	11	0	0	0	0	0
Necrosis	0	10	0	3	5	5*
P.M.N., exudate	0	11	0	3	2	0
Granuloma formation	0	6	1	10	0	0
Encysted oil droplets	0	6	6	10	0	0
Calcium deposits in nerve	0	9	0	0	5	0

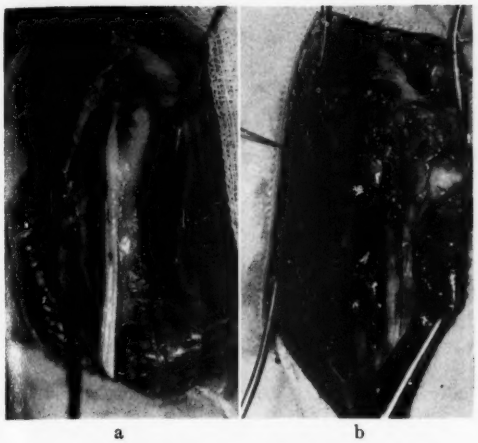
*Very slight change in 2 experiments.

proximal half of each thigh was exposed for a distance of about 5 centimeters. In this way the effects of two different substances could be compared in each animal. Great care was taken to avoid traumatizing the nerve. In each instance 0.5 cubic centimeter of the sterile material to be studied was injected. In some of the dogs, 0.5 cubic centimeter of the same material was injected into the center of a hamstring muscle at a distance from the nerve injection, and the site of injection marked with a silk suture for future identification. A 20 gauge needle was used for both the intraneural and intramuscular injections. The wound was then closed with silk sutures. One dog developed a wound infection and is not included in these experiments. All animals were observed for evidence of impairment of function of the muscles innervated by the sciatic nerve. The animals were sacrificed 2 to 58 days after injection and autopsy was performed immediately. Cultures were taken from several of the wounds and none of these exhibited any evidence of the growth of bacteria. Gross pathological changes were noted and specimens of nerve and muscle were removed for fixation in formalin and in Zenker's solution. The sections were stained with hematoxylin and eosin and, in some cases, by Kossa's silver nitrate method for calcium.

TABLE II.—INTRAMUSCULAR INJECTION

Type of material	Isotonic NaCl	Calcium penicillin, oil and wax	Peanut oil	Beeswax and peanut oil
No. experiments	2	7	6	10
Duration, days	7–14	5–36	5–42	2–58
Macroscopic changes Normal	2	0	0	0
Necrosis and exudate	0	4	0	3
Droplets of oil	0	3	6	7
Microscopic changes Normal	2	0	0	0
Necrosis	0	4	0	3
P.M.N. exudate	0	4	0	3
Granuloma formation	0	4	1	7
Encysted oil droplets	0	0	6	0
Calcium deposits	0	6	0	0

A commercial preparation of calcium penicillin in peanut oil and beeswax was injected into the nerve in 12 experiments and into the muscles in 7. This was composed of 4.8 per cent U.S.P. white beeswax in peanut oil with 300,000 units of calcium penicillin per 1 cubic centimeter. Beeswax and peanut oil combined were used in 11 nerve and 10 muscle injections. This consisted of the same proportions of these two substances as used in the commercial product. Peanut oil alone was



a b

Fig. 1. a, Normal appearance of sciatic nerve and hamstring muscle cut in cross section, 14 days after the injection of isotonic sodium chloride solution into muscle (left) and nerve. b, Local enlargement and discoloration of sciatic nerve and necrosis of hamstring muscle cut in cross section (arrows), 7 days after the injection of calcium penicillin in peanut oil and beeswax.

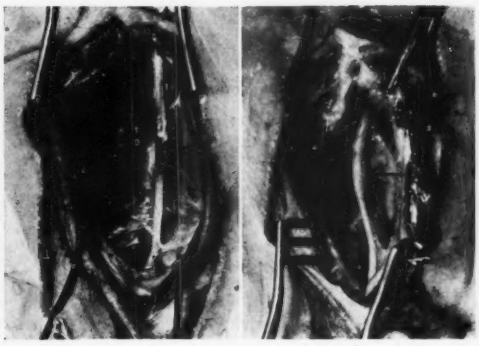
injected into the nerve in 6 and into the muscle in 6 experiments. Calcium or sodium penicillin was used in a solution of isotonic sodium chloride prepared immediately before injection. This solution contained 300,000 units of either the calcium or sodium salt of penicillin per 1 cubic centimeter. Each of these penicillin salts, without oil or wax, was injected into 5 nerves. As a control, an isotonic solution of sodium chloride alone was injected intraneurally in 11 and intramuscularly in 2 experiments.

RESULTS

The results of all experiments are summarized in Tables I and II.

Clinical observations. Neither sodium chloride nor peanut oil produced significant paralysis when injected into the sciatic nerve (Table I).

On the other hand, severe paralysis which persisted until termination of the experiments was produced in many instances by intraneural injection of sodium penicillin alone, beeswax and peanut oil, calcium penicillin, and calcium penicillin in beeswax and oil, in order of increasing frequency and severity.



a b

Fig. 2. a, Local necrosis and discoloration of the sciatic nerve (arrow) 18 days after the injection of calcium penicillin. b, Local enlargement of the sciatic nerve (arrow) 28 days after the injection of peanut oil and beeswax.

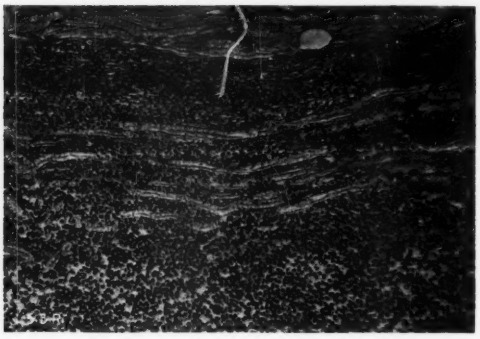
Gross pathology. Injection of saline solution into the sciatic nerve in 11 experiments and into muscle in 2 experiments resulted in no significant gross pathologic change in any instance (Fig. 1 a).

On the other hand, injection of calcium penicillin in oil and wax resulted in marked changes in both nerve and muscle. At all periods, from 2 to 36 days after injection, the nerves were found to be locally enlarged, adherent to surrounding tissues, and usually discolored (Fig. 1 b). In 7 of 12 nerves gross necrosis of the nerve was evident. In 4 of 7 muscle specimens, gross necrosis and exudate were present. In the remaining 3, oil droplets with local swelling were seen.

Peanut oil alone produced only minimal gross abnormalities in both nerve and muscle. Two of 6 nerves showed local enlargement and adhesions at the site of injection. In all of the 6 muscle specimens, residual droplets of oil were grossly visible on section, varying from 5 to 42 days after injection.

Peanut oil and beeswax (without penicillin) produced the same enlargement of the nerve as when penicillin was included in the injected substance, but gross necrosis and discoloration were absent (Fig. 2 b). In muscle, local necrosis was visible in 3 of 10 instances and only oil droplets could be seen in the remainder.

Injection of calcium penicillin alone into the sciatic nerve produced acute necrosis



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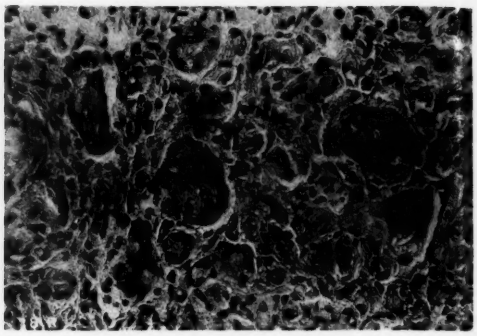

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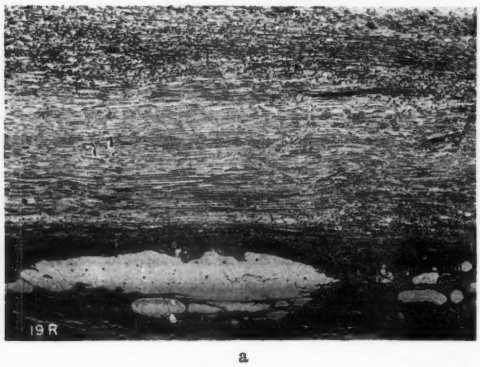
Fig. 3. a, Sciatic nerve showing the polymorphonuclear exudate present 2 days after the injection of calcium penicillin in peanut oil and beeswax. Hematoxylin and eosin ×105. b, Granuloma in the sciatic nerve 21 days after the injection of the same material. Hematoxylin and eosin ×185.



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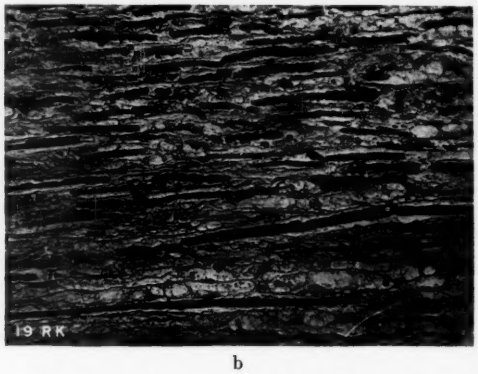

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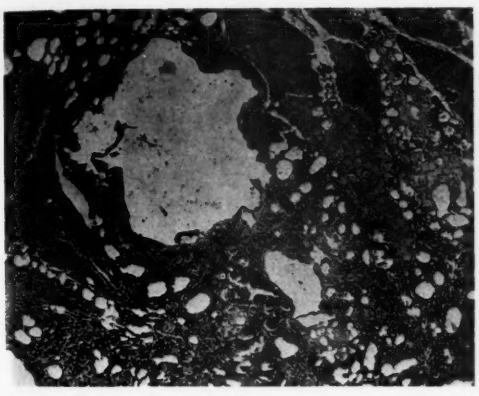
Fig. 4. a, Sciatic nerve 28 days after injection of calcium penicillin in peanut oil and beeswax. Upper third of photograph shows a bland type of inflammatory reaction. Middle section of photograph shows necrosis with axons appearing as small black rods. Lower third of photograph shows the granuloma in the epineural tissues. Hematoxylin and eosin ×30. b, The appearance of the axons in the same nerve. Kossa's silver nitrate method for calcium ×200.

without local enlargement (Fig. 2 a), and sodium penicillin alone resulted in a lesser degree of necrosis in 3 of 5 nerves.

Microscopic pathology. Microscopically, no significant change was demonstrable in either nerve or muscle after injection of saline solution.

However, injection of calcium penicillin in oil and wax produced striking microscopic changes (Table I). Immediate necrosis of nerve fibers was observed, concomitant with prompt infiltration of the nerve trunk at the site of injection by polymorphonuclear leucocytes (Fig. 3 a). In the center of the injected area, these changes were so profound as to result in almost complete loss of continuity of the nerve. Toward either end, however, the essential architecture of the nerve was preserved, although axons were necrotic and fragmented. The epineurium was infiltrated with inflammatory cells and was necrotic in the central area.

Following this earliest effect, the acute inflammatory reaction gradually gave way to the infiltration of mononuclear cells, fibroplasia, especially in the perineurium, formation of giant cells, and development of granulomatous lesions in the nerve and its sheath (Figs. 3 b and 4 a). These "chronic" effects, together with the persistence of encysted



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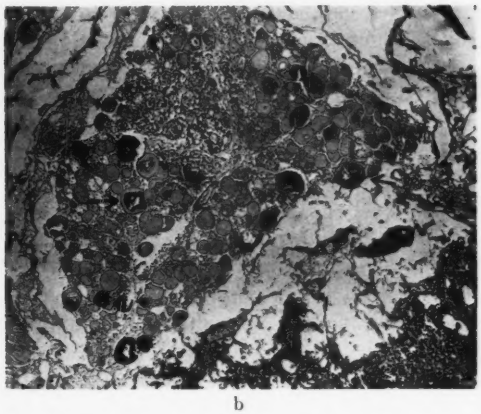

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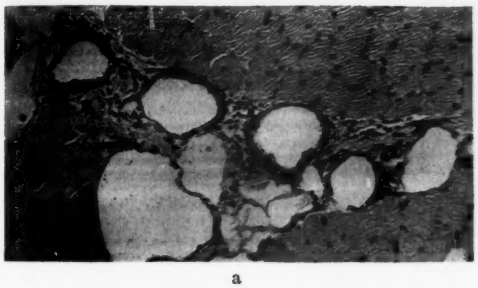
Fig. 5. a, Granuloma produced in muscle 36 days after the injection of calcium penicillin in peanut oil and beeswax. Hematoxylin and eosin ×55. b, Section of muscle showing necrosis and polymorphonuclear exudate 5 days after injection of same material. Note deposit of calcium in muscle fibers (arrows). Hematoxylin and eosin ×160.



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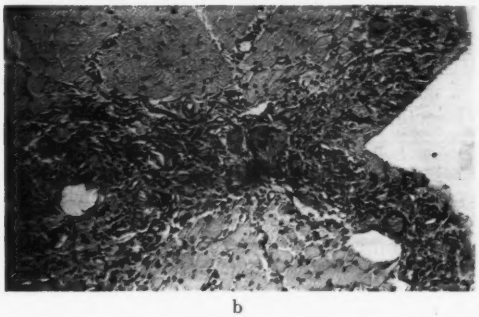

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Fig. 6. a, Section of muscle showing mild mononuclear infiltration and small cystic spaces lined with mononuclear cells produced by the injection of peanut oil 7 days previously. Hematoxylin and eosin ×125. b, The granulomatous reaction produced by the injection of peanut oil and beeswax 58 days previously. Hematoxylin and eosin ×100.

droplets of oil, were most marked in the third and fourth weeks and persisted throughout the duration of the longer experiments.

Meantime, deposits of calcium appeared in the rod-like areas earlier occupied by the fragmented and necrotic axis cylinders. Whether they replaced or were deposited in the fragments of axons could not be determined, but their appearance as short, irregular rods was most striking, particularly in sections stained by Kossa's silver method for calcium (Fig. 4 b).

Injection of the same preparation of calcium penicillin in oil and wax into muscle produced very similar changes (Table II). Necrosis of muscle and acute inflammatory exudate were followed by formation of granulomas (Fig. 5 a) and deposit of calcium in necrotic muscle fibers (Fig. 5 b). These changes persisted throughout the longest experiments (36 days), and, in the latter, the granulomatous areas had become partially encapsulated by dense fibrous tissue.

When peanut oil alone was injected into either nerve or muscle, necrosis, acute inflammation, and granuloma formation were not observed. Oil droplets became encysted by mononuclear cells and persisted throughout the duration of all experiments (Tables I and II, Fig. 6 a).

However, injection of beeswax in peanut oil (without penicillin) into the sciatic nerve resulted in moderate necrosis in only 3 of 11 experiments, but in extensive granulomatous changes in 10 of the 11 nerves.

Similarly, oil and wax produced granulomas in 7 of 10 injected muscles (Fig. 6 b), but necrosis and acute inflammation in only 3.

Injection of either calcium penicillin or sodium penicillin alone into the nerve resulted in some degree of necrosis and destruction of nerve fibers in all experiments (the changes were less marked in the experiments with sodium penicillin). In addition, all nerves injected with calcium penicillin showed the characteristic deposits of calcium in the fragmented axis cylinders.

COMMENT

It is apparent from these experiments that specific pathologic changes may be attributed to the various substances which were injected. Thus granulomatous changes occurred only when beeswax was contained in the substance injected. Necrosis of nerve and muscle occurred with greatest frequency and severity when calcium penicillin was injected, but was produced to a lesser degree by both sodium penicillin (in nerve) and beeswax. Deposits of calcium in nerve and muscle were observed only when calcium penicillin was included in the injected substance.

The mechanism and significance of the deposit of calcium within necrotic axons and necrotic muscle fibers are not clear, but may throw light upon other physiologic and pathologic processes involving deposition of calcium.

It seems justifiable to point out certain probable clinical implications of these observations. Although parenteral systemic penicillin injections should, of course, be intramuscular, it is surprising that more clinical difficulties have not resulted from injuries to nerves, blood vessels, tendons, and other structures by such injections. Our experiments indicate that calcium penicillin alone may be highly injurious to nerves and is by no means innocuous when injected into muscle. The injurious effect of sodium penicillin upon nerves seems much less severe.

Since many, if not most, penicillin injections are administered by nurses or technicians, it is highly important that these individuals, as well as physicians, be impressed with the importance of injecting penicillin only into the thicker portions of muscles which are far removed from important nerve trunks.

The effects of injections of calcium penicillin in peanut oil and beeswax observed in our experiments not only emphasize the importance of avoidance of nerves, but cast serious doubt upon the wisdom of injecting this preparation into muscle.

SUMMARY

A case is cited in which extensive necrosis of the radial nerve occurred following an injection of calcium penicillin in peanut oil and beeswax.

In experiments upon dogs, injections of this preparation or its separate components or of sodium penicillin or of sodium chloride solution were made into the sciatic nerve or a hamstring muscle or both, with the following results:

1. Sodium chloride produced no effects.
2. Sodium penicillin produced mild or moderate necrosis of nerve fibers.
3. Calcium penicillin produced extensive necrosis of both nerve and muscle with deposition of calcium in fragmented axons and necrotic muscle fibers.
4. Peanut oil produced only a mild monocytic reaction with encystment of fat droplets.
5. Beeswax in peanut oil produced extensive granulomatous inflammation with minimal necrosis in both nerve and muscle.
6. Calcium penicillin in oil and wax produced, in marked degree, a combination of the pathologic changes which resulted from injection of its component parts.

The possible clinical implications of these observations are discussed.

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ANGIOCARDIOGRAPHY IN THORACIC SURGERY

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THE method of angiocardiography introduced in 1938 by Robb and Steinberg (7) consists of roentgenographic visualization of the chest at appropriate intervals following the rapid intravenous injection of a substance which is radiopaque. In this manner the innominate veins, the superior vena cava, the right atrium and ventricle, the pulmonary artery and its branches, the pulmonary veins, the left atrium and ventricle, and the thoracic aorta and its brachiocephalic branches may be rendered sufficiently opaque to distinguish them from the surrounding structures. This delineation takes place in a progressive fashion and demonstrates quite clearly the size, exact location, and configuration of all the cardiac cavities and larger vascular lumina in the mediastinum and lungs.

While this method has many applications, it is particularly valuable in the diagnosis and in the planning of surgical attack on mediastinal and pulmonary lesions. Thus, various vascular anomalies, such as patent ductus arteriosis, coarctation of the aorta, infundibular and pulmonary stenosis, aberrant pulmonary veins, congenital pulmonary artery aneurysm, may be clearly demonstrated as has been brought out in other investigations (3, 5, 6, 9, 10). It is the purpose of this presentation to indicate the value of this method in the diagnosis and treatment of nonvascular lesions of the mediastinum and lung which may be amenable to surgical treatment.

By means of angiocardiography mediastinal tumors may not only be outlined but their relations to adjacent cardiovascular structures clearly defined (12, 13). This is of tremendous significance both in gauging the operability of a given tumor and in aiding the surgeon to avoid certain complications. It is safe to say that the most decisive single factor in the successful extirpation of a mediastinal tumor is its separation from large vessels or parts of the heart with which it may be in intimate contact. It is this element in the operation about which the surgeon feels most concern, and indeed a very large portion of the operative mortality in such cases has been due to hemorrhage secondary to accidental entry into a large vessel or one of the atria. In avoiding this catastrophe the surgeon has been hampered heretofore by two factors. First, the tumor may have produced marked distortion of large blood vessels not discernible on the conventional films and these may therefore be inadvertently entered during the freeing of a mediastinal tumor. Secondly, as the presenting and lateral borders of the growth are freed the dissection reaches a point very often when the tumor itself, if it be of any size, lies between the surgeon and the point of dissection, and thus conceals the exact nature of the structures being freed except as they may be identified and localized by palpation. It can readily be seen how great an aid to the surgeon would be the exact demonstration of the configuration of the tumor and its relations to the heart and great vessels which may be obtained by means of angiocardiography.

Visualization of the pulmonary artery and vein indicates not only the normal relations of these vessels and the presence of anomalies such as abnormal derivation of arteries or of veins (2, 4), but by showing the effects of lesions in the obliteration or distortion of major pulmonary vessels at the hilum (11) may influence the surgeon in deciding on the operability of a given lesion and in planning the surgical attack upon it. Enough experience has not yet been gained with this method to permit decisions as to operability to rest upon the findings brought out by it alone (8, 14), but this report will illustrate some of the ways it has proved useful and in which its evidence has been checked by operation.

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This investigation was aided by a grant from the Schering Corporation.

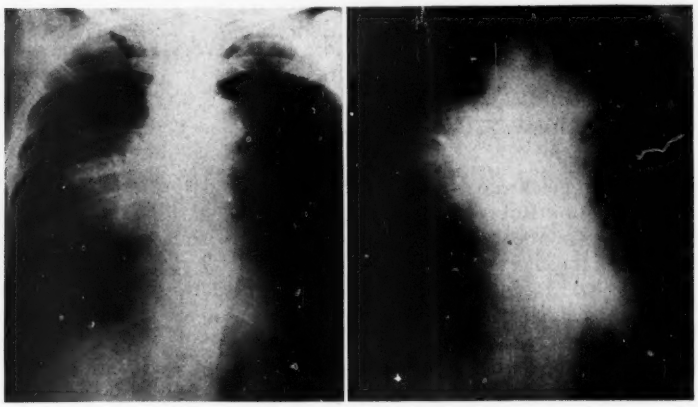

Fig. 1. Case 1. Aortic aneurysm. a, left, Conventional frontal roentgenogram. Heart apparently normal. Note large ovoid mass near right hilum and prominent aortic knob. b, Frontal angiocardiogram. Saccular aneurysm of ascending aorta and fusiform aneurysm of transverse aorta. Note thick wall of aneurysm which prevented pulsation.

THE DIFFERENTIAL DIAGNOSIS OF THORACIC ANEURYSM

The history, physical signs, and appearance on conventional x-ray examination of aortic aneurysms and mediastinal neoplasms may be so similar that in the past it occasionally has been possible to establish a definite diagnosis only when thoracotomy has been undertaken. By means of angiocardiography, however, this distinction is made with relative ease since, when aneurysm is present, its lumen is outlined by means of the opaque medium except in cases in which it is filled with clot or when in a saccular aneurysm the opening of the sac is quite small. Even under these circumstances, however, the presence of other angiocardiographic evidence of abnormalities of the aorta with which aneurysm may be associated give support to the diagnosis. Thus, in syphilitic aortitis dilatation of the ascending aorta and irregularity of its lumen may be evident with or without aneurysm, while arteriosclerotic changes or congenital abnormalities apt to be associated with aneurysm are made much more clearly recognizable when the lumen of the aorta is outlined with opaque media.

The value of angiocardiography in differentiating aortic aneurysm and mediastinal tumor is illustrated in the following 2 cases.

CASE 1. A 45 year old negro chauffeur complained of a feeling of constriction in the throat and gradually increasing dyspnea of 6 months' duration. He had had a penile sore 30 years previously and his blood Wassermann was positive at the time of this examination. The physical signs were limited to dullness and diminished breath sounds over the anterior aspect of the right chest. Conventional roentgenogram (Fig. 1a) showed a large ovoid mass extending from the hilum into the right lung field, and on lateral projection this was seen to lie in the anterior mediastinum. The aortic knob was prominent and on fluoroscopic examination no pulsation could be detected in the mass.

Angiocardiography (Fig. 1b) revealed the contrast medium in the central part of the shadow in question and dilatation of the aortic arch leading to a diagnosis of luetic aortitis with saccular aneurysm arising from the ascending portion of the arch. This method also showed the wall of the aneurysm to be 1.5 centimeters thick, suggesting the presence of laminated thrombus and explaining the absence of pulsation.

CASE 2. This case was similar in many particulars to the foregoing and involved a 38 year old negro who, though without symptoms, was found in the course of routine x-ray examination of his chest to have a mass projecting into the right lung field and adjacent to the right cardiac border. He too gave a history of a penile lesion many years previously and his blood Wassermann was positive. Physical signs were similar to those in the previous case.

Conventional roentgenography (Fig. 2a) revealed an anterior mediastinal mass extending outward from the right border of the cardiac shadow, its lateral margin sharply demarcated and its rim containing calcific deposit. On fluoroscopy the mass showed a pulsation synchronous with cardiac systole.

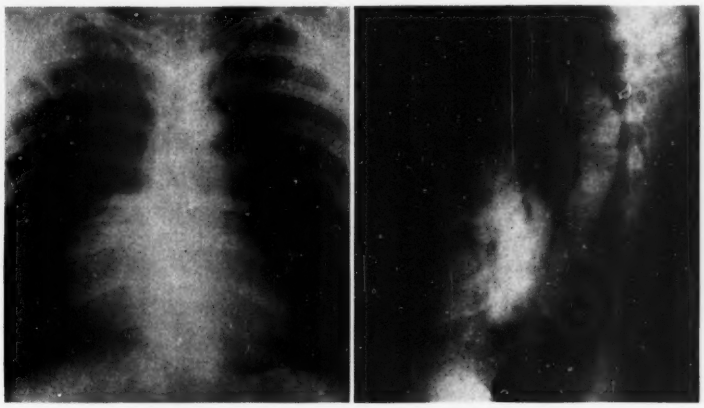

Fig. 2. Case 2. Mediastinal dermoid cyst. a, left, Conventional frontal roentgenogram. Note right paracardiac mass with border containing calcium. Fluoroscopy demonstrated pulsation. b, Left anterior oblique angiocardiogram. Normal left heart and aorta visualized. Mass is shown to be nonvascular.

Angiocardiographic studies (Fig. 2b) outlined an aortic arch which appeared entirely normal and none of the opaque material entered the suspicious mass. These facts, therefore, pointed to the presence of a neoplasm of the anterior mediastinum, the contour of which suggested that it was benign, and when taken with its location and the presence of calcification indicated that it was probably a dermoid cyst. The diagnosis in this case was confirmed at operation and the tumor was successfully removed.

Following the diagnosis of aneurysm in Case 1, an attempt at wiring was made in another hospital but the patient succumbed after operation from bronchopneumonia.

While it is true that evidence to be obtained from routine studies makes the differentiation between aneurysm and mediastinal tumors possible in many instances, angiocardiography is an extremely valuable method not only confirming or modifying evidence obtained by such methods but in some instances being the sole means at present whereby this distinction can be made aside from surgical exploration. The 2 cases cited with identical histories of primary lesions and serological findings, with similar shadows in conventional x-ray films, and with one mass showing no pulsation while the other was deceptively pulsatile, indicate some of the difficulties. Angiocardiography promptly cleared up the matter, however, and in addition yielded detailed information as to the site of origin of the aneurysm and offered an explanation of the absence of characteristic pulsation in the thickness of its wall. Aside from clearly demonstrating that the mass in the second case was not an aneurysm, thereby pointing the evidence such as configuration, site, and the presence of a calcified rim in the conventional films toward a diagnosis of dermoid cyst, it also yielded valuable information concerning the size and location of the tumor and its relation to neighboring cardiac and vascular structures.

MEDIASTINAL TUMORS

In view of the embryological development of the mediastinal structures involving as it does the descent of the diaphragm and the heart from a more cephalad origin while the lower respiratory tract and esophagus are being formed, it is not surprising that a number of tumors should be found in this region whose origin is best explained on the basis of misplaced embryonic rests. These include the dermoid cysts, others derived from the primordium of the bronchi and lungs, the so-called bronchogenic cysts, and still others arising in connection with the pericardium. While the dermoids are most often found in the anterior part of the superior mediastinum, they are also encountered near the hilum of the lung or in other locations intimately associated with the heart and great vessels, showing

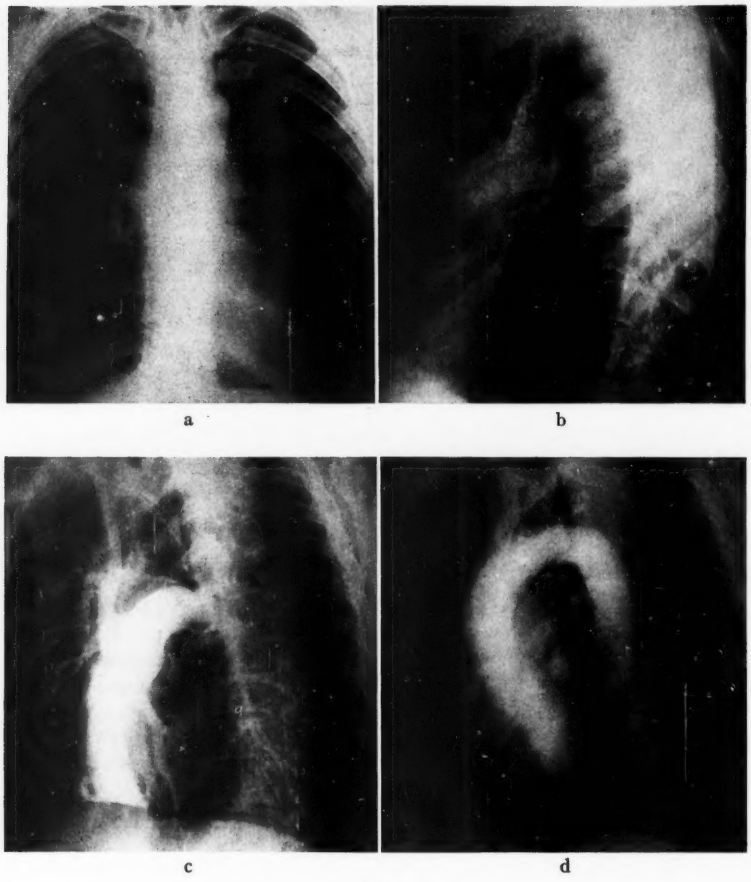

Fig. 3.
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the latter characteristic with the bronchogenic cysts. Solitary echinococcus cysts of the mediastinum, unassociated with dissemination of the infestation involving also the liver or lungs, are quite rare but may occur through direct spread from the intestinal tract by way of the retroperitoneal and posterior mediastinal lymph channels.

In all of these types of cysts visualization of the chambers of the heart and of the great vessels is of considerable value both in determining the exact location of the cysts and their relations to the surrounding structures. Even before angiocardiography became available the general location of a mediastinal tumor was recognized as being important in its differential diagnosis, but the delineation of the mass was limited to portions protruding into the lung fields or deforming identifiable portions of the trachea or esophagus. Otherwise, the borders of the tumor were indistinguishable from the normal mediastinal structures.

By means of angiocardiography, borders of tumors in contact with the venae cavae, with parts of the heart and great vessels, and any pressure effects in these structures are clearly shown. Benign tumors even though small

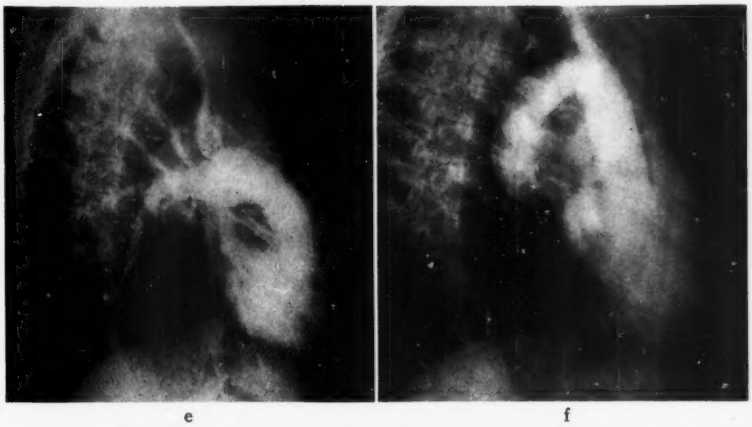

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Fig. 3. Case 3. Mediastinal dermoid cyst. a, Conventional frontal roentgenogram. Heart normal. Note mass at upper right heart border. b, Conventional left anterior oblique roentgenogram. Note rounded mass below aortic window. c, Left anterior oblique angiocardiogram. Displacement of the superior vena cava to the right and the left pulmonary artery toward the left. Note deformity of right auricular appendage. d, Left anterior oblique angiocardiogram. Left atrium, left ventricle and entire aorta are normal. Note mass within aortic arch. e, Right anterior oblique angiocardiogram. Intact right ventricle and pulmonary artery. Note anterior displacement of right branch of pulmonary artery. f, Right anterior oblique angiocardiogram. Entire left heart and aorta normal. Note nonopacified mass occupying aortic window.

may cause marked compression or dislocation of the mediastinal vessels, malignant tumors may constrict or obliterate them, while still other neoplasms such as the lipomas and some thymomas of a softer consistency may insinuate themselves between the vessels so that even when reaching considerable size they cause few evidences of compression.

Dermoid Cyst

CASE 3. N.Y.H. No. 363569. An asymptomatic 44 year old policeman was found to have a mediastinal mass on routine roentgen examination of the chest. History and physical examination were noncontributory. Chest roentgenograms in frontal view (Fig. 3a) revealed a shadow projecting a short distance from the right mid-cardiac border which could not be distinguished from the cardiovascular silhouette medially. In the left oblique view (Fig. 3b) a rounded density was seen to occupy the aortic window and to displace the esophagus posteriorly. These findings were interpreted as representing a mediastinal tumor although the presence of an aneurysm could not be excluded.

Angiocardiography was performed in right and left anterior oblique projections so as to obtain a three dimensional study of the lesion. Films made at 2½ seconds after injection (Fig. 3c, e) revealed opacification of intrinsically normal right atrium and ventricle. The opacified superior vena cava was seen to be displaced to the right by the mass, while the right branch of the pulmonary artery was displaced anteriorly and the left branch was displaced toward the left. Films made at 8 seconds (Fig. 3d, f) revealed intrinsically normal left atrium, ventricle, and aortic arch. The mass was not opacified and could easily be outlined by reference to the opacified surrounding vascular structures. It was clearly shown to be partly within the circle of the aortic arch, causing displacement of the pulmonary arteries and the superior vena cava, and in intimate relation inferiorly to the pulmonary veins and the left atrium. A diagnosis of dermoid cyst was made and a difficult surgical procedure predicted on the basis of its intimate vascular relationship.

This was confirmed at operation. After opening the right pleural cavity a bulging mass could be seen presenting between the vena cava and the trachea and dislocating the azygos vein superiorly. It was obviously cystic in nature and the sac was opened and a considerable quantity of fluid and grumous material was evacuated from it. Further dissection was carried out by placing a finger within the cavity and freeing the cyst wall as one would a hernia sac. This was so densely adherent to the atrium and the vena cava that portions were left *in situ* and the cavity remaining packed with oxycel. The patient made an uneventful recovery. Examination of the specimen revealed striated muscle, both transitional and ciliated epithelium.

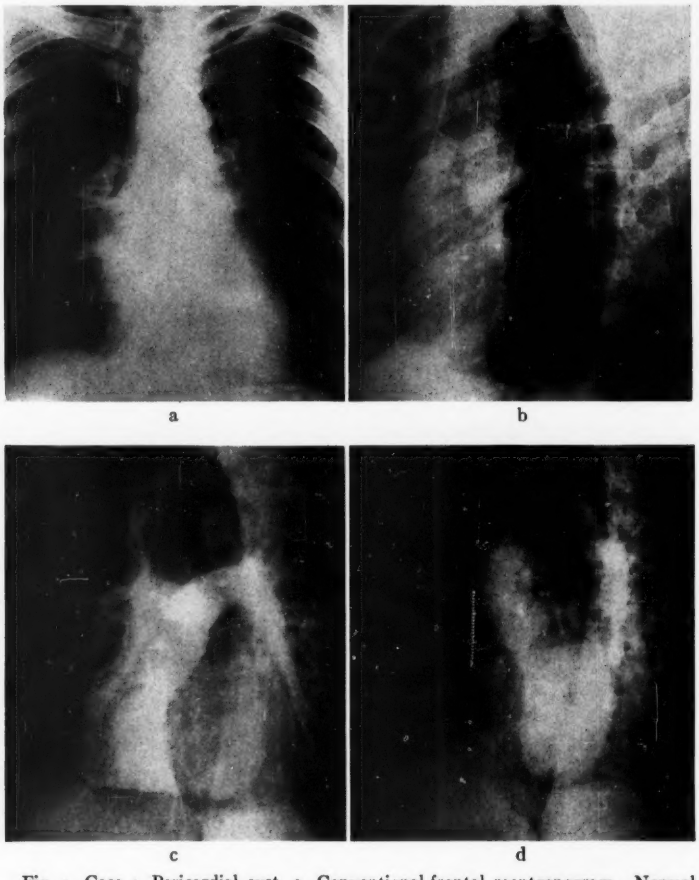
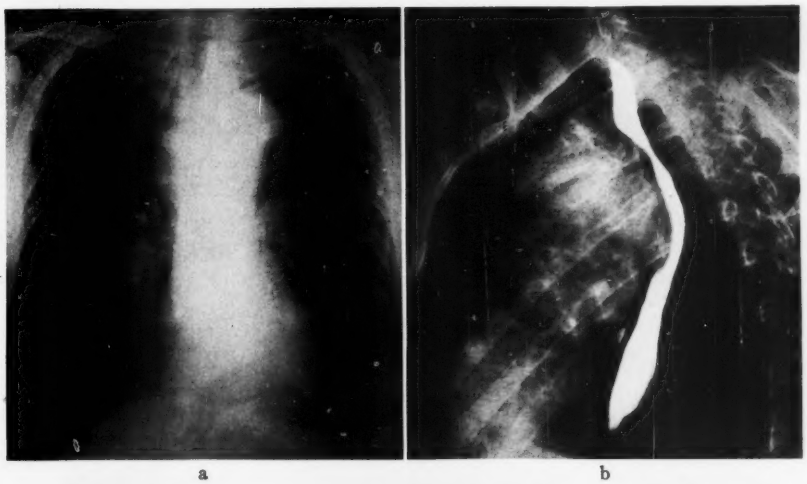


Fig. 4. Case 4. Pericardial cyst. a, Conventional frontal roentgenogram. Normal cardiac outline save for bulge in upper right heart border. b, Conventional left anterior oblique roentgenogram. Normal cardiac outline except for prominence in upper anterior cardiac border. c, Left anterior oblique angiocardiogram. Note displacement of superior vena cava, right auricular appendage, and the pulmonary conus. Right heart, pulmonary artery and its branches are otherwise normal. d, Left anterior oblique angiocardiogram. Left heart and aorta intact, excluding aneurysm of sinus of Valsalva.

Pericardial Cyst

CASE 4. N.Y.H. No. 503554. Another tumor appearing in conventional films to be in a similar location was seen in a 44 year old high school teacher. He was without symptoms but was found to have an abnormal prominence along the right cardiac border. Physical examination revealed only a precordial systolic murmur and routine laboratory studies were not contributory. Conventional frontal and left anterior oblique chest roentgenograms (Fig. 4a, b) revealed the shadow of a mass, projecting anteriorly and to the right of the heart. Its outer border was sharply defined, while medially it could not be distinguished from the heart.

An angiocardiogram made at 2 seconds following injection (Fig. 4c) showed posterior displacement of the superior vena cava and an extrinsic pressure defect of the pulmonary conus. Both of these findings could have been the result of an aneurysm of the sinus of Valsalva, a possibility which was excluded by a 10 second film (Fig. 4d) showing an entirely normal aortic arch. Anterior mediastinal tumor closely related to the right upper cardiac border, probably a dermoid or pericardial cyst, was diagnosed.



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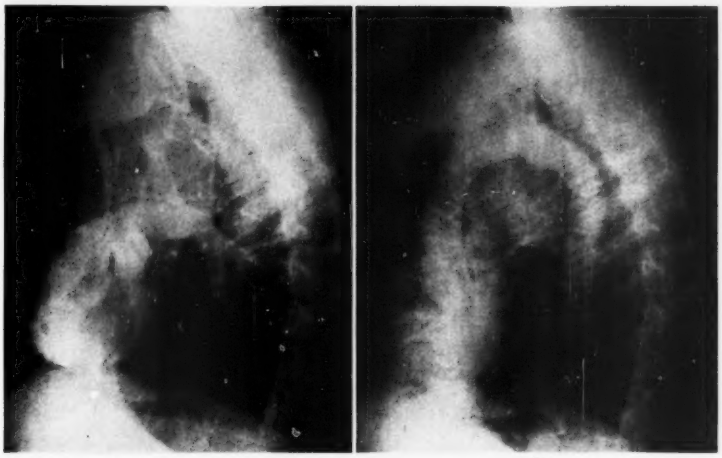


c d

Fig. 5. Case 5. Bronchogenic cyst. a, Conventional frontal roentgenogram. Note widening in region of ascending aorta with narrowing and displacement of trachea to right. b, Left anterior oblique esophagram. Esophagus is displaced posteriorly. c, Left anterior oblique angiocardiogram. Superior vena cava, right heart, pulmonary artery and branches are intact. d, Left anterior oblique angiocardiogram. Left heart and aorta normal, excluding aortic aneurysm. Note that mass lies beneath aortic arch.

At operation a pericardial cyst was found presenting in front of the vena cava and compressing this structure posteriorly. The cyst measured approximately 10 by 6 by 6 centimeters and was somewhat loculated, one process extending deeply into the mediastinum and being attached to the pericardium over the auricle.

Angiocardiography in this case showed the relation of the cyst to the vena cava and the pulmonary conus, thereby indicating a somewhat different location than the preceding tumor, and also indicating its intimate connection with the pericardium.

Cysts arising from the primordium of the respiratory tract may be found both in the superior mediastinum and in association with the major bronchi. Their walls occasionally

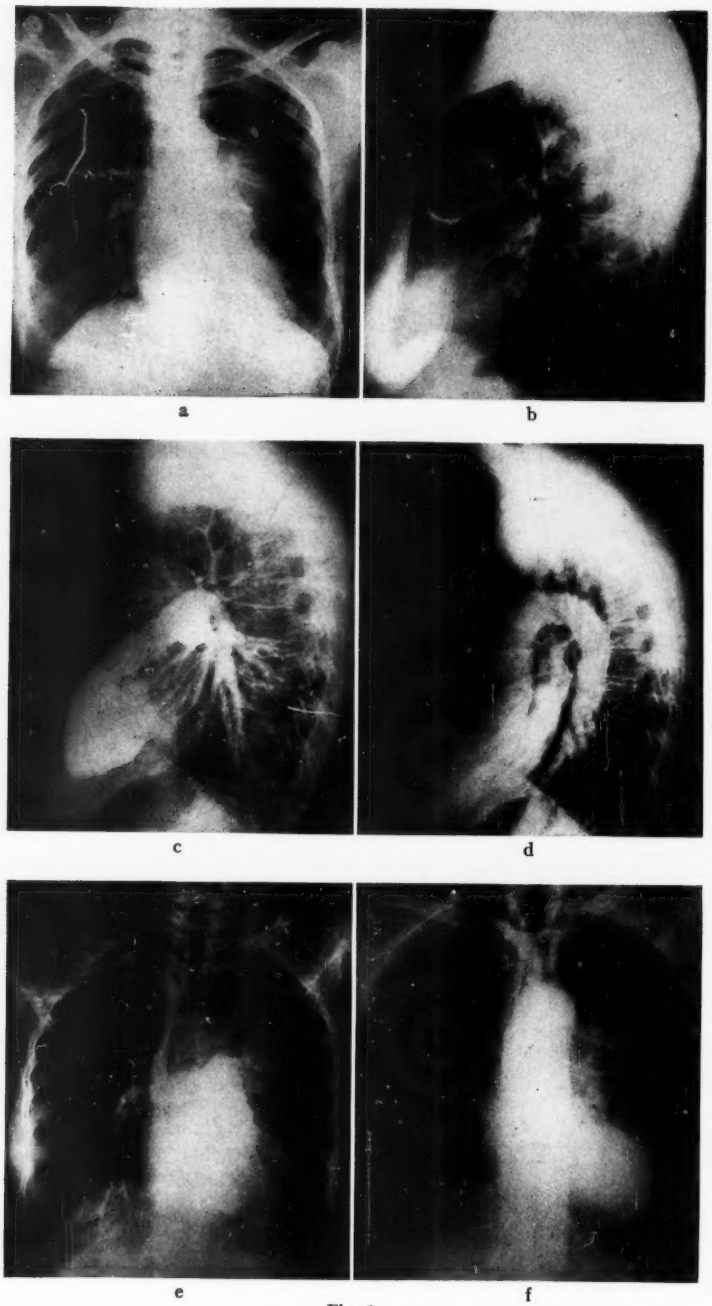


Fig. 6.
(*Legend on opposite page.*)

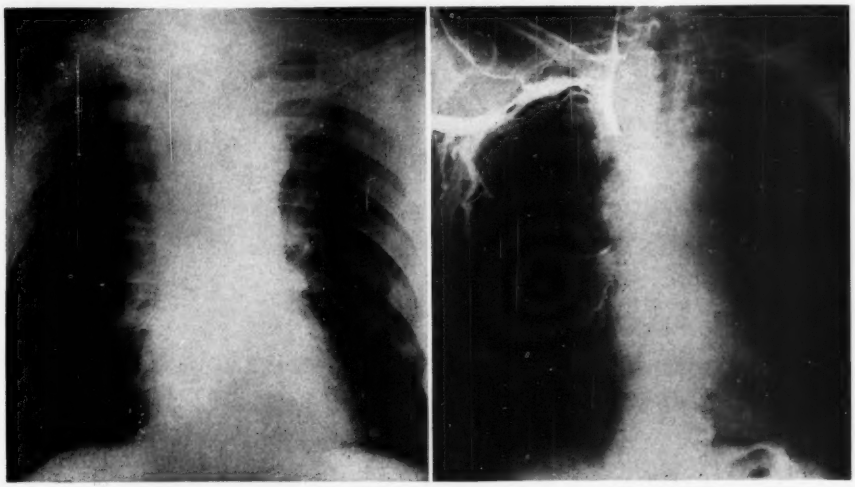


Fig. 7. Case 7. Lymphoma. a, left, Conventional frontal roentgenogram. Note widening of right upper mediastinum. b, Frontal angiocardiogram. Note stenosis of right subclavian and innominate veins with complete occlusion of superior vena cava and resulting collateral circulation.

contain cartilage and are lined with ciliated or transitional epithelium, and the cysts, filled with clear or murky fluid, usually cast a shadow in the x-ray film of about the same density as the surrounding mediastinal structures and their contour is only revealed as they project into a lung field or dislocate the trachea or major bronchi. They sometimes reach considerable size but even when relatively small may cause some pressure symptoms, and as in other mediastinal tumors angiocardiography may be of aid in both their diagnosis and treatment, as in the following case.

Bronchogenic Cyst

CASE 5. N.Y.H. No. 512041. A 50 year old white male was admitted complaining of hoarseness of 3 weeks' duration. His history revealed that he was well until 3 months before admission, at which time he noticed the onset of progressively increasing dyspnea and 1 month previously noted the onset of hoarseness which progressed to the point where his voice was reduced to a whisper. Physical examination was unrevealing save for the finding of paralysis of the left vocal cord. Routine laboratory studies were negative. Conventional frontal and left anterior oblique roentgenograms of the chest (Fig. 5a, b) revealed the presence of a mass which could not be separated from the aorta and which displaced the trachea to the right and anteriorly and the esophagus posteriorly. It had the appearance of an aneurysm of the aortic arch.

Angiocardiographic studies (Fig. 5c, d) showed normal right and left cardiac chambers and no evidence of abnormality of the aortic arch. The mass was seen to be partially encircled by the aorta, and a diagnosis of benign superior middle mediastinal tumor was made. This was supported by the solitary nature of the mass—the sharply delineated borders, the fact that it was not connected with the aorta and had neither invaded nor produced stenosis of any of the major blood vessels.

At operation a simple bronchogenic cyst was found similar in size and location to that in Case 3. It contained about 150 cubic centimeters of milky fluid and was removed. Because of its relations with the esophagus and the air passages, part of the mass could be outlined, but it remained for angiocardiography to reveal the displacement of the vena cava and to show that the mass had no connection with the aorta. Demonstration before operation of its intimate contact with the atrium and the vena cava was important in planning and carrying out the dissection which finally freed it from these structures since they lay behind the tumor and could be seen

Fig. 6. Case 6. Thymoma. a, Conventional frontal roentgenogram. Note large mass adjacent to aortic knob. b, Conventional lateral roentgenogram. Note anterior rim of mass which contains calcium. c, Lateral angiocardiogram. Entire right heart, pulmonary artery and branches which are normal. d, Lateral angiocardiogram. Left heart and aorta are also normal, thereby excluding the presence of an invasive tumor. e, Frontal angiocardiogram. Normal superior vena cava, right atrium, right ventricle, pulmonary artery and branches. f, Frontal angiocardiogram. Left cardiac chambers and aorta opacified and shown to be separated from tumor mass.

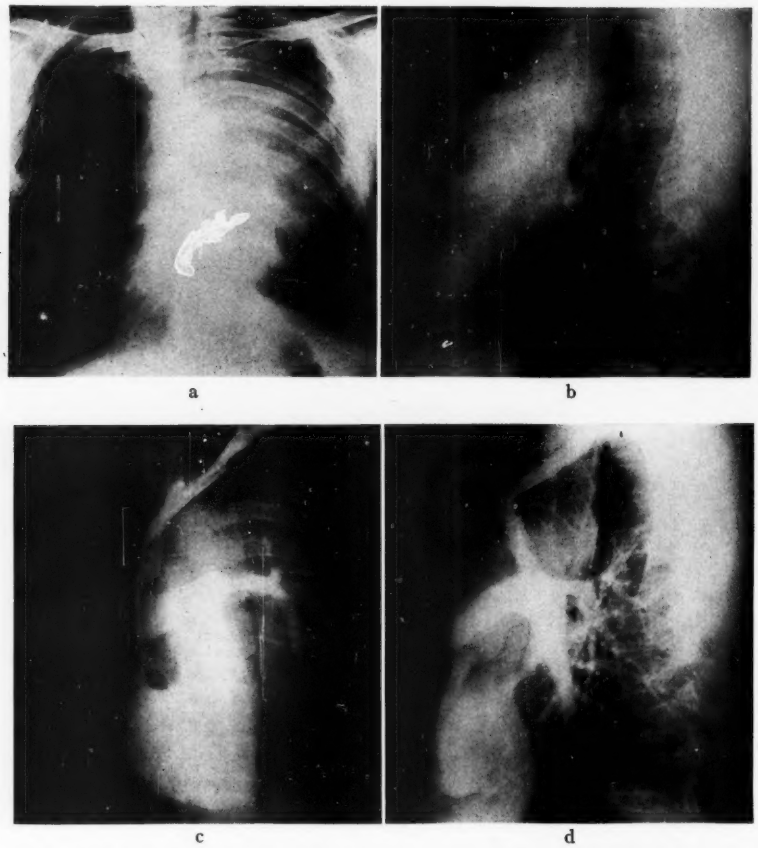


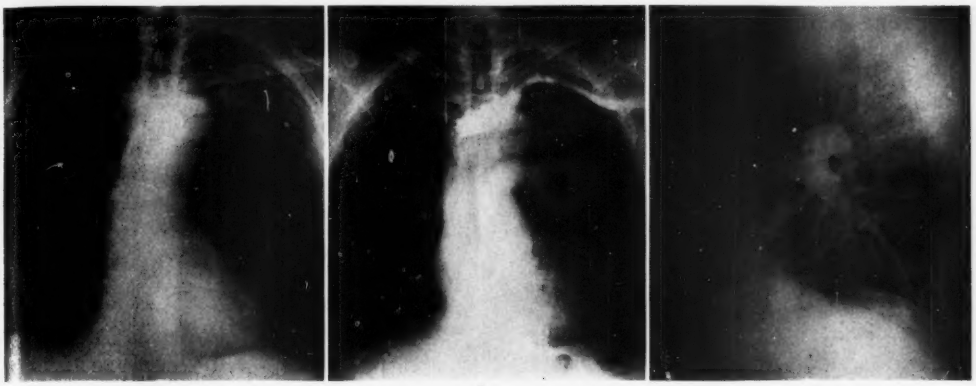
Fig. 8. Case 8. Bronchogenic carcinoma. a, Conventional frontal roentgenogram. Note most of the left lung field occupied by dense mass. b, Conventional lateral roentgenogram. Mass occupies most of left upper lung field. c, Frontal angiocardiogram. Superior vena cava, right atrium and ventricle, mainstem pulmonary artery and right pulmonary artery are normal, whereas the left pulmonary artery is narrowed and stenotic. d, Lateral angiocardiogram. Note contour of superior vena cava, right heart chambers, pulmonary artery. These and the right pulmonary artery are normal, in contrast to the narrowed left pulmonary artery, evidence of hilar presence of tumor. Pulmonic valve cusps are demonstrated.

only at operation after the cyst had been largely removed.

Thymic Tumors

The thymus may be the seat of a variety of tumors, including both those whose origin may be traced to its normal component cells and others, such as dermoid cysts and teratomas arising from misplaced embryonic rests. The former group comprises the lymphosarcomas and others composed of epithelial elements classified under the general term of thymomas. Some of these are encapsulated even though their internal typography and cellular characteristics may be those of malignancy, while others are highly invasive and metastasize to the neighboring cervical and mediastinal nodes and elsewhere.

No group of mediastinal tumors varies so much in the effects which they produce on surrounding structures. Some are small and produce little or no true pressure effects although they may cause some dislocation of



a b c

Fig. 9. Case 9. Pulmonary tuberculosis simulating bronchogenic carcinoma. a, Conventional frontal roentgenogram. Circumscribed density, left upper lung field. b, Frontal angiocardiogram. Normal right heart, pulmonary artery and branches. Note elevation of left pulmonary artery and avascularity of left upper lobe. c, Lateral angiocardiogram. Right heart and pulmonary artery intact. Right pulmonary artery normal; left pulmonary artery displaced upward with avascularity of terminal branches.

the vessels in the superior mediastinum. Others, though well encapsulated, because of their location may compress the veins and cause obvious distortion of the trachea or esophagus; while a third group, truly malignant, surrounds the superior mediastinal structures producing critical compression symptoms and bringing about the death of the patient from strangulation. Angiocardiography is particularly valuable in this group of tumors since the conventional films often show little beyond the presence of a mass in the anterior mediastinum, and it is the relation to the great vessels and pericardium and atria in which the clinician, and particularly the surgeon, is most vitally interested.

CASE 6. N.Y.H. No. 462473. A 54 year old housewife who had been known to have an anterior mediastinal mass for 7 years developed the symptoms of myasthenia gravis a year before her admission to the hospital. A previous course of x-ray therapy had had no effect upon the size of the mass, and recently it had grown larger and the patient began to lose weight. Physical examination revealed generalized muscle weakness thought typical of myasthenia gravis, and save for a precordial systolic murmur, examination of the chest was unremarkable. Laboratory studies included a basal metabolic rate of −2 per cent and a creatinine tolerance test showing 60 per cent excretion. Conventional roentgenogram (Fig. 6a, b) revealed an irregular anterior mediastinal mass projecting from the left hilar region anteriorly. The mass contained calcium and was roentgenoscopically observed to pulsate.

Angiocardiographic studies in the frontal projection showed normal right heart and pulmonary arterial filling at 2¼ seconds (Fig. 6e) and normal left heart and aortic filling at 8 seconds (Fig. 6f). The mass did not fill with opaque medium. Lateral studies (Fig. 6c, d) similarly timed showed intrinsically normal cardiovascular structures and failed to reveal opacification of the tumor mass. A diagnosis of anterior mediastinal tumor was made and its operability predicted. In this case, besides ruling out gross involvement of the great vessels, particularly that of the left pulmonary artery, contrast visualization revealed the tumor to be posteriorly bounded by the pericardium, and clearly defined its hitherto concealed relations and boundaries.

At operation a firm nodular tumor, approximately 8 centimeters in diameter, was found in intimate relation to the pericardium and pulmonary vessels. On pathological examination the tumor was well encapsulated but microscopic study showed it to be completely unlike normal thymus and to contain many mitotic figures, leading to a diagnosis of small celled thymoma, probably malignant.

Tumors of the Mediastinal Nodes

The term lymphoma is employed to designate the various tumors of the mediastinal nodes including Hodgkin's disease and lymphosarcoma. These conditions exhibit their tendency to multiple sites of involvement here as elsewhere, but may often simulate in their symptomatology and physical and conventional x-ray findings other mediastinal tumors for which surgery is indicated. While films taken in various projections or therapeutic

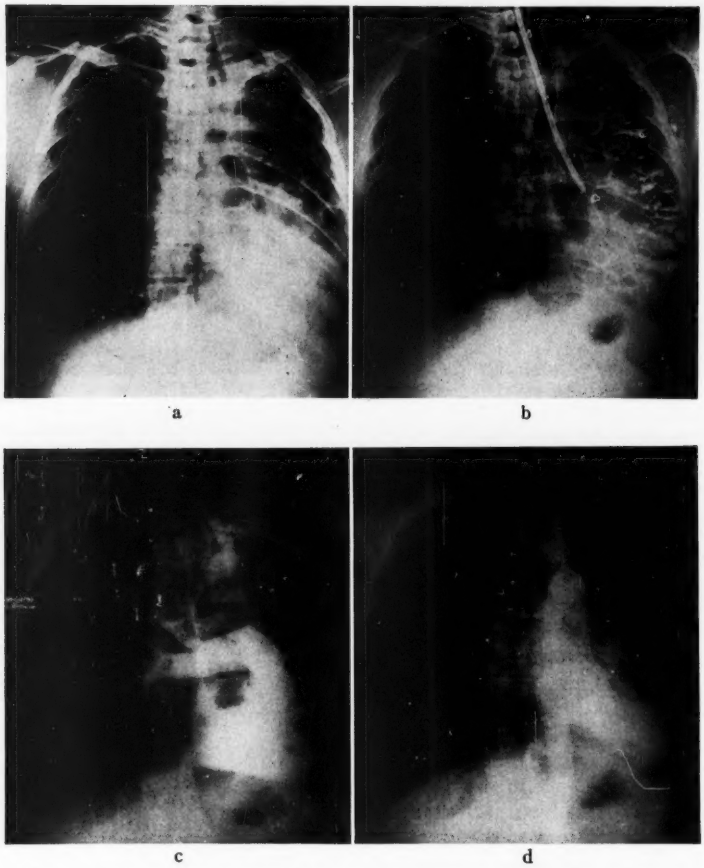


Fig. 10. Case 10. Bronchiectasis, left lung, with mediastinal retraction. a, Conventional frontal roentgenogram. Note extensive fibrosis of left lung with multiple cavities and tracheal deviation toward the left. The heart cannot be delineated. b, Frontal bronchogram. Catheter in left main bronchus with filling of saccular and cystic bronchiectatic cavities. c, Frontal angiocardiogram. Note angulation of left subclavian and innominate veins with displacement of superior vena cava into left chest. Heart rotated into right anterior oblique position with enlargement of right pulmonary artery and branches, finer radicles of which pass over the midline into the left chest. Note avascularity of left lung. d, Frontal angiocardiogram. Left heart and aorta rotated into right anterior oblique view but otherwise normal. The heart has become truly "visible" after opacification.

test doses of radiation when added to other laboratory examinations may establish the diagnosis in many instances, angiocardiography is often of additional aid. Thus, multiple mediastinal or hilar masses may be encountered in various types of infections including tuberculosis and Boeck's sarcoid as well as in the lymphomas, but demonstration of invasion of the superior vena cava or other vascular structures of the mediastinum by means of angiocardiography suggests a malignant process. In addition, this method provides much information as to the site and configuration of the occlusive process, whether due to dislocation, compression, constriction, or actual invasion of the vessels.

CASE 7. N.Y.H. No. 378034. A 73 year old male complained of substernal pain of 1 week's duration. The history disclosed that there had been swelling of the face, neck, and hands during the preceding 2 months as well as a gradually increasing dysphagia. Physical examination revealed marked venous congestion of the head, neck, upper extremities and collateral vessels over the lateral chest wall. Laboratory studies showed a marked elevation of the venous pressure in the arms and an arm-to-tongue circulatory time of 40 seconds—a marked delay. Conventional roentgenogram (Fig. 7a) revealed widening of the superior mediastinum to the right by a lobulated mass extending down to the right hilum. On lateral study this was seen to be located in the anterior mediastinum.

Angiocardiography confirmed the clinical impression of superior vena caval obstruction as films made 4 (Fig. 7b) and 12 seconds after injection showed multiple rounded filling defects in the right innominate vein and superior vena cava causing complete occlusion. There was opacification of extensive collateral channels, including anterior intercostal veins and those of the lateral thoracic wall which were tortuous and dilated due to the obstruction. Insufficient radiopaque material passed or by-passed the point of obstruction to produce opacification of right heart or pulmonary vessels at 4 seconds, in contradistinction to the normal cycle as shown in the preceding cases.

The angiocardiographic evidence was that of a diffuse neoplastic process in the anterior mediastinum causing obstruction to the great veins of the superior mediastinum with occlusion of the superior vena cava, and a diagnosis consistent with lymphoma was made. Following a course of radiation therapy the mass became smaller, the patient's clinical signs of superior vena caval obstruction disappeared. Repeat angiocardiograms, while still showing filling defects in the superior vena cava, showed no collateral circulation and at 4 seconds there was normal opacification of the pulmonary arteries.

The confirmation of the clinical signs of superior vena cava obstruction and the demonstration of its site as well as of multiple rounded filling defects suggested a tumor involving multiple nodes as the cause. The favorable response to x-ray therapy supports this conclusion.

BRONCHOGENIC CARCINOMA

With the diagnostic methods now available, including routine x-ray examinations, bronchoscopy, and the cytological study of sputum or bronchial washings, a positive diagnosis of carcinoma of the lungs or bronchi can be made in about 85 per cent of the cases. In the remainder the diagnosis can only be determined after thoracotomy. Although the tumor has reached an inoperable stage in many instances before diagnosis is made, the number of cures over a period of 5 years or longer has now reached an encouraging figure.

In assembling information in a given case of proved or suspected bronchogenic carcinoma the data to be obtained from angiocardiography may be of both diagnostic and prognostic significance. Thus, by visualization of the vascular structures of the mediastinum, hilar lymph node enlargement due to metastases or vascular stenosis which may indicate encroachment of malignant tissue can sometimes be demonstrated. Occasionally, changes in the pulmonary vascular pattern may serve to localize a peripheral tumor or other lesion. In still other cases in which carcinoma is suspected demonstration of elevation or kinking of a vessel may serve to suggest an inflammatory or cicatricial as opposed to a neoplastic process.

While we have been much impressed with the aid to be obtained by such a demonstration or confirmation of lymph node metastases and depicting of pulmonary vascular occlusions in indicating inoperability, it cannot be said that a sufficient experience has yet been gained to deny a patient the possible benefits of operation on such evidence alone.

CASE 8. N.Y.H. No. 314521. A 54 year old Italian male was admitted who complained of chest pain which had been present for 3 years but had become worse during the previous year and was associated with dyspnea, cough, and weight loss.

Physical examination was unremarkable save for dullness and absent breath sounds over the upper left chest and for clubbing of the fingers. All laboratory tests were noncontributory, and bronchoscopy revealed narrowing of the left main bronchus due to external pressure. Conventional x-ray films showed a large homogeneous density projecting into the left lung field and seen on lateral films to lie anteriorly (Fig. 8a, b). This was interpreted as a benign mediastinal tumor. Angiocardiographic studies in frontal (Fig. 8c) and lateral projections (Fig. 8d) made at 2½ seconds after injection showed normal right atrium and ventricle but the pulmonary artery before its bifurcation was dilated as was its right branch. The entire left pulmonary artery was distorted and narrowed as though encircled by tumor. On the basis of these findings inoperability was suggested and this was confirmed at operation, and later at autopsy when a primary bronchogenic carcinoma was identified.

CHRONIC PULMONARY INFLAMMATION

In the preceding case stenosis of the pulmonary artery was demonstrated; in many others complete obstruction of a main branch or of the artery itself may be seen. Both these findings strongly suggest a malignant tumor, but as with other laboratory tests the clinical picture as a whole must be considered. Pulmonary tuberculosis in its chronic stage may cause apparent or real diminished vascularity in the involved portion of a lung, or contraction of the scar tissue may bring about distortion or angulation of hilar vessels which must be differentiated from tumor, as illustrated by the following case.

Pulmonary Tuberculosis

CASE 9. N.Y.H. No. 507826. A 48 year old male was admitted complaining of dull aching chest pain and chronic cough for 2 years' duration. Physical examination was noncontributory. Conventional chest roentgenogram (Fig. 9a) showed an ill-defined, ovoid area of mottled density in the anterior apical segment of the left upper lobe from which streaks extended to the hilum. Repeated sputum examinations for tubercle bacilli were negative. Bronchoscopic examination revealed "extrinsic pressure, left main bronchus."

Angiocardiogram made 3 seconds after injection in frontal projection (Fig. 9b) revealed a normal right heart and right pulmonary artery. The left pulmonary artery was elevated and its superior branch could not be seen. A lateral examination confirmed these findings. The angiocardiographic diagnosis was "these findings are not regarded as conclusive, but should the area of infiltration actually represent a malignant tumor, the odds are that it is an inoperable one."

At operation a firm mass was palpated in the left upper lobe which was firm but not stony hard. No hilar nodes could be found. The differentiation was obviously between a chronic inflammatory process and a tumor, and it was decided to perform a lobectomy with the idea of examining the mass immediately. This revealed fibrocaseous tuberculosis, and the man made an uneventful recovery.

This and other cases indicate that in interpreting the significance of angiocardiographic distortion or even failure of filling of pulmonary vessels, it must be borne in mind that such effects do not necessarily indicate malignancy but may be produced by chronic inflammatory processes, including tuberculosis or other lesions. Thus, we have seen failure of filling of a major branch of the pulmonary artery due to pressure from a large tuberculous hilar node, and in another instance observed marked reduction in circulation to one lung in association with the atelectasis caused by a pedunculated chondroma of a bronchus. This last is in line with the experimental evidence (1) indicating marked reduction in pulmonary circulation in the presence of atelectasis.

In chronic pulmonary infections such as bronchiectasis the angiocardiograph may yield valuable information regarding alterations in the anatomy and in the circulatory dynamics.

Bronchiectasis

CASE 10. N.Y.H. No. 507495. A 31 year old male was admitted who complained of cough productive of a pint of sputum a day. The past history revealed 3 attacks of pneumonia and an unusual susceptibility to upper respiratory infection, and on physical examination dullness and loud course rales over the entire left chest were elicited. Sputum contained mixed flora on culture. Conventional roentgenogram (Fig. 10a) showed extensive chronic pleural thickening over the left chest with multiple honeycombed areas throughout the lung field. The heart and mediastinum had shifted into the left chest and bronchography (Fig. 10b) revealed extensive cystic bronchiectasis of the left lung.

Angiocardiography in the frontal projection timed to show the right heart and pulmonary arteries (Fig. 10c) revealed a shift of the heart into the left chest. The heart had rotated about 45 degrees in a counterclockwise direction. The left branch of the pulmonary artery did not opacify while the right branch was seen to be well filled and dilated. There also seemed to be an increase in the number of branches to the right lung and some of these branches were seen to cross into the left chest, conclusive evidence of the presence of herniation of the right lung into the left chest.

The dislocation of the heart and other mediastinal structures associated with fibrous changes in chronic pulmonary suppuration which can be visualized on fluoroscopic examination or on conventional films has long been recognized, but with angiocardiography the changes in the vascular patterns can also be demonstrated. These changes are seen to consist not only in dislocation of the vessels but in their actual occlusion and to have brought about a marked diminution in vascularity of the involved lung.

SUMMARY AND CONCLUSIONS

Our experience with angiocardiography in thoracic surgery has included such cases as

have been presented here involving aneurysms, dermoid, pericardial and bronchogenic cysts, thymic tumors, the lymphomas, bronchogenic carcinoma, and chronic pulmonary inflammation including tuberculosis and bronchiectasis. In the study of any thoracic surgical problem we have found this to be a most important ancillary method and the information which it yields has been of great value in diagnosis, in determining operability and in the planning and carrying out of the surgical attack. Further evaluation is still needed and the data obtained by angiocardiography are most valuable when added to the results of routine x-ray studies including fluoroscopy, conventional roentgenograms in various positions, and esophagrams and bronchograms when indicated.

The demonstration of its safety in over 1,000 cases, both medical and surgical, in our hands shows it to be a method which should be used as a routine, save in the few instances in which contraindications, such as known sensitivity to iodine containing radiopaque compounds or severe renal disease, are present.

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A CONSIDERATION OF THE CAUSES OF DEATH FOLLOWING OPERATION FOR CONGENITAL HEART DISEASE OF THE CYANOTIC TYPE

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THE operation originally described by Blalock and Taussig and the variant described by Potts, Smith, and Gibson have in common the establishment of an artificial ductus arteriosus in patients with a diminished circulation to the lungs resulting from pulmonary stenosis or atresia. Between November 30, 1944, and September 25, 1947, 500 patients with congenital heart disease and cyanosis were operated upon in the Johns Hopkins Hospital by Dr. Alfred Blalock and his associates with the intention of creating an artificial ductus arteriosus. Dr. Blalock has recently described his experience with these patients and the anatomical variations encountered (3). An evaluation of the various procedures performed must be delayed since it entails a prolonged study of the postoperative condition of these patients. Such an evaluation is in progress (18). It seems helpful, however, to study those cases which terminated fatally during this period.

When the present investigation was undertaken we hoped to elicit some correlation between the pathological data and the preoperative, operative, and postoperative clinical observations. In this respect the investigation has been disappointing. Only in recent years has the disturbed physiology in patients with congenital cyanotic heart disease been elucidated by cardiac catheterization (5, 6, 7), angiocardiography (8, 16), and studies of blood volume (12) and renal blood flow (15). In our present state of ignorance concerning the "normal" physiology of this group of patients it is no wonder that difficulty is encountered in attempting to correlate the findings of the clinician with those of the pathologist. In spite of this difficulty some observations on the course and the cause of death of individual patients may be helpful to others who are interested in the treatment of this disease.

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TABLE I.—CAUSES OF DEATH

	Number of patients	Per cent mortality
Cerebral complications	22	4.4
Arrhythmia during operation	21	4.2
Cardiac failure and pulmonary edema	15	3.0
Hemorrhage	7	1.4
Thrombosis of the anastomosis	5	1.0
Respiratory complications	4	0.8
Shock	2	0.4
Miscellaneous and unexplained	23	4.6
	99	19.8

Of the first 500 patients 99 are dead at this writing, a mortality rate of 19.8 per cent. These 99 patients can be divided into arbitrary but fairly definite groups according to a clinical evaluation of the primary cause of death. This grouping is helpful by emphasizing complications of which one must be aware and is as follows (Table I): (1) cerebral complications, (2) arrhythmia during operation, (3) cardiac failure and pulmonary edema, (4) hemorrhage, (5) thrombosis of the anastomosis, (6) respiratory complications, (7) shock, and (8) miscellaneous and unexplained causes. In the last group are included several patients who died of incidental disease such as leukemia, meningitis, and pneumonia.

Cerebral complications (Table II). Twenty-two, or 4.4 per cent, of the 500 patients had signs of damage to the central nervous system as the primary complication. These signs consisted of: (1) failure to respond following the anesthesia or lapse into coma after initial response, (2) convulsions, unilateral or generalized, or (3) pronounced disorientation. There were often additional signs of neurologic dis-

ease. That this is the commonest cause of death is to be expected when one realizes that these patients live with low arterial oxygen saturation and considerable polycythemia. Both of these conditions make the brain more susceptible to the ill effects of cardiorespiratory and circulatory derangements occurring during operation. In almost all instances the difficulty was initiated by a period of cerebral ischemia or anoxia, usually during the operation. In some patients there was pre-existing cerebral damage.

Although the clinical course of these patients was that associated with damage to the central nervous system, in only 11 of the 22 patients was there pathological confirmation of this diagnosis; H.L. (No. 73) was the only patient who had massive thrombosis of the right carotid artery. This extended into the circle of Willis and presumably resulted from ligation of the carotid artery at its origin from the innominate. C.W. (No. 195) had a past history of a cerebrovascular accident. Autopsy disclosed left parietal cerebral atrophy in addition to more recent small superficial cortical hemorrhages. W.B. (No. 234) exhibited no signs of cerebral disturbance and was progressing satisfactorily until 1 month after operation. Autopsy showed extensive old encephalomalacia with recent, apparently spontaneous, thrombosis. M.S.V. (No. 249) had multiple small thrombi in the corpus striatum and the right and left occipital cortices. In this instance there was considerable cerebral anoxia since the left and main pulmonary arteries thrombosed after an unsatisfactory anastomosis. K.M. (No. 284) gave a history of former right hemiplegia. After operation left hemiplegia developed associated with a fresh right cerebral infarction. B.J.L. (No. 388) had been retarded mentally following meningitis 6 months before admission and had slight left facial paralysis. Autopsy showed a large abscess of the left temporal lobe. No anastomosis was performed on B.A.W. (No. 329) because of 5 periods of pronounced bradycardia. At autopsy the brain was seen to be edematous with fresh infarcts, cerebral softening, and flattening of the convolutions from edema and pressure attributed to the ischemia associated with the bradycardia. There were some old cerebral scars with deposits of hemosiderin as well as more recent small hemorrhages. In G.T. (No. 445) there was chronic meningitis which had not been suspected from his history or physical examination. In those whose cerebral damage must have occurred preoperatively, one assumes that the additional anoxia and cerebral ischemia at operation were sufficient to damage the brain irreparably.

Three other patients showed slight pathological evidence of cerebral damage. In B.R.E. (No. 63) there was only suggestive evidence of thrombosis of the cerebral sinus in that there "seemed to be a cerebral venous obstruction." R.M. (No. 198) had a small hemorrhage in the upper left frontal cortex and J.T. (No. 325) showed several small parietal hemorrhages on the right.

In the 11 remaining patients there were no pathological signs of intracranial lesions. However, further studies by the methods reviewed by Hoff, Grenell, and Fulton may shed more light on the causes of death in these instances. Such studies are in progress.

Cerebral vascular thrombosis is a common cause of death in untreated patients with cyanotic congenital heart disease. In the majority of patients in this group, however, search for such lesions was fruitless. In at least the 11 patients without pathological evidence of cerebral damage, death was probably due to cerebral anoxia from a low arterial oxygen saturation, or to cerebral ischemia caused by occlusion of a carotid or innominate artery, or to bradycardia. It will be shown later that most instances of pronounced bradycardia are due to anoxemia.

Nineteen of these 23 patients had at least one of the following conditions in common: severe cardiac arrhythmia, the use of the carotid or the innominate artery in the anastomosis, or a history of pronounced symptoms of disturbances to the central nervous system. Of the 4 patients remaining, 1 became unusually cyanotic during the operation, 1 had hypotension for 10 minutes associated with brisk hemorrhage, 1 with Cooley's anemia had mild bradycardia early in the operation, and the fourth had tracheal compression from a retroesophageal subclavian artery. The last death would at present be preventable.

TABLE II.—CEREBRAL COMPLICATIONS

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
C.R. 7	18 years F	Moderate	Mentally slow	Extreme cyanosis. Typical tetralogy	70	LI, ES. Slight arrhythmia early	Unresponsive second day. Rt. hemiparesis appeared	Not done
G.M. 10	4½ years M	Extreme	Chronic otitis	Large heart	41	RI, ES. Marked cyanosis	Response poor. Convulsions	Tetralogy. Extreme stenosis
W.D. 17	21 mos. M	Moderate	Typical tetralogy	Extreme cyanosis	58	RI, ES. 30 c.c. laked blood given I.V. Severe arrhythmia twice	Never responded	Transposition of the great vessels
C.D. 22	4½ years M	Mild	Previous meningitis. Had convulsions with spells	Large heart moderate cyanosis	38	RS, EE to branch to upper lobe. Bradycardia	Poor response	Tetralogy, moderate stenosis
B.R.E. 63	3 years F	Mild	Spastic on right. Old cerebral hemorrhage	Slight left facial paralysis	35	RS, ES. Cyanosis marked once	Poor response	Tetralogy. Evidence of cerebral venus obstruction
H.L. 73	2 years M	Moderate	Recent otitis media	Heart slightly large, mild cyanosis	48	RI, ES. Early bradycardia	Left hemiplegia on waking	Tetralogy. Thrombosed rt. carotid through circle of Willis
G.M. 89	2 years F	Moderate	Negative	Pronounced cyanosis. Left axis deviation by EKG	16	RI, ES. Heart weak early	Did not respond. Left hemiplegia	Single ventricle, pulmonary stenosis
C.W. 195	4½ years F	Extreme	CVA 9 mos. previously. Convulsions with spells. Mentally slow	Typical tetralogy	45	RS, ES.	Did not respond	Tetralogy. Left parietal atrophy. Several small recent cortical hemorrhages
R.M. 198	5 years M	Moderate	Negative	Typical tetralogy	45	RS, ES. Marked cyanosis twice	Did not respond. Spastic. Given heparin	Tetralogy. Small hemorrhage, left frontal cortex
M.C. 208	15 years F	Moderate	Negative	Typical tetralogy	60	RC, ES to branch to upper lobe	Did not respond. Left-sided convulsions	Tetralogy with atresia. Anastomosis to branch to right upper lobe
G.S.M. 225	4 years F	Extreme	Frequent "spells"	Typical tetralogy	47	RC, ES. Cardiac action poor during anastomosis	Left hemiplegia on 2d day. Later rt. sided convulsions	Not done
J.M. 228	5 years F	Moderate	Stuporous with spells	Typical tetralogy	64	RC, ES. Cardiac arrest 5 times	Left weakness	Tetralogy. Pulmonary hemorrhage and edema
W.B. 234	12 years M	Moderate	Negative	Small for age. Cardiac decompensation. Digitalized	20	Large RS, ES. Heart never strong. Stimulants several times	Improved for 1 month. Cerebral signs last day	Extensive old encephalomalacia. Transposition of great vessels, pulmonary stenosis. Small interventricular septal defect
M.L. 236	7 years M	Mild	Cooley's anemia	Large heart, liver and spleen. Digitalized	19	RS, ES. Bradycardia early	Did not respond	Tetralogy
M.S.V. 249	4 years F	Mild	Unconscious on one occasion	Typical tetralogy	61	RS, EE. Tiny pulmonary artery	Convulsions on 2d day	Tetralogy with atresia. Main and left pulmonary arteries thrombosed
K.M. 284	15 mos. F	Severe	Right hemiplegia	Heart slightly large. Left axis deviation by EKG	13	RC, ES. Slight arrhythmia on occlusion of pulmonary artery	Responded poorly. Left hemiplegia	Tricuspid and pulmonary atresia. Recent and old right encephalomalacia. Anastomosis and carotid artery thrombosed

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

TABLE II.—CEREBRAL COMPLICATIONS—Continued

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
J.T. 325	2 years F	Mild	Negative	Typical tetralogy	25	Retroesophageal, RS, ES.	Poor response. Convulsions and right sided spasticity on 2d day	Tracheal and esophageal constriction. Several left parietal cortical hemorrhages
B.A.W. 329	4 years F	Moderate	Occasional spells of unconsciousness	Heart slightly large	53	Bradycardia 5 times. No anastomosis	Did not respond	Tetralogy. Brain edematous, fresh infarcts, cortical softening
B.J.L. 388	10 years F	Mild	Mentally slow since meningitis 6 mos. before	Typical tetralogy. Right-sided weakness	56	LS, ES. Extrasystoles early	Responded poorly. Increase in right paresis. Given heparin	Typical tetralogy. Large left temporal lobe abscess. Actinomyces seen
I.C. 394	2 years F	Moderate	Convulsions and coma with spells	Dextrocardia	39	LS, ES. Asystole during incision, responded to stimulants	Never awoke. Convulsions	Not done
G.T. 445	12 years M	Mild	Fainting spells	Typical tetralogy. Small for age	89	RS, ES. 10 minute period of hypotension after hemorrhage	Hypotension. Pulmonary edema, temp. 104°	Tetralogy. Meningitis, gram positive cocci
F.H. 443	5 years M	Moderate	Probable CVA at 2 and 4 yrs.	Typical tetralogy. Chronic otitis	23	LS, ES. Bradycardia 2 times on closure of skin	Response poor	Tetralogy. Thrombus in anastomosis

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

Gross and Ware have shown that retrotracheal or retroesophageal vessels may cause tracheal or esophageal obstruction, especially if there is an obliterated vessel to complete the vascular ring around these structures. In 22 of the first 500 patients such an anomalous vessel was present but was unassociated with symptoms of obstruction. However, following the use of a retroesophageal vessel in performing a pulmonary artery anastomosis, a smaller ring is created and in at least 1 patient there was evidence of tracheal obstruction after operation. Recently it has been thought advisable in some cases to transpose the retroesophageal vessel to a position anterior to the bronchus on the side operated upon before doing the anastomosis. Since this plan has been followed there has been no known obstruction.

Measures which will reduce the mortality due to cerebral damage are directed toward maintenance of adequate cerebral circulation and oxygenation. These include maintenance of arterial blood pressure, of forceful and regular heart action, and of full pulmonary ventilation. Aside from the obviously essential replacement of blood volume lost during the operation, oxygenation of arterial blood is probably basically more important than other factors. This may best be effected by a high concentration of oxygen in the anesthetic mixture, sufficient "assist" by the anesthetist to keep all but the upper lobe on the side operated upon expanded and functioning, and inflation of the lung during rest periods placed at intervals short enough to prevent pronounced cyanosis (2). Although the mediastinum must be reasonably quiet during the performance of the anastomosis, it is important to keep the patient as lightly anesthetized as possible. During periods of hypotension it is advisable to lower the head of the table.

Although the use of the innominate or carotid artery may be advisable in order to provide a suitable vessel for anastomosis, the risk is increased thereby. One of these vessels was used in 10 of the 23 patients in this group. Because of the added risk the carotid artery has rarely been ligated in the more recent patients. Occasionally it may be occluded temporarily during approximation of a short subclavian and the pulmonary arteries during performance of the anastomosis.

The risk is also greater in patients with a history suggesting damage to the central nervous system, such as convulsive "spells," pro-

nounced mental retardation, hemiplegia, or mastoiditis or intracranial infection. Robbins has demonstrated that there is a significantly increased incidence of brain abscess in patients with congenital heart disease and cyanosis, and one should be aware of this probability in patients with a history of middle ear or intracranial infection.

In some instances the cerebral damage was associated with factors that should be avoidable. W.D. (No. 17) was mistakenly given 30 cubic centimeters of whole blood in distilled water by intravenous infusion. C.D. (No. 22) and M.C. (No. 208) had unsatisfactory, very small anastomoses performed because the branch of the pulmonary artery to the upper lobe was mistakenly used in each case. In the presence of many collateral vessels in the mediastinum and hilum of the lung one hesitates to do more dissection than is necessary, but it is advisable to free the pulmonary artery enough to see clearly the branches to the middle and lower lobes and thus be sure that the entire pulmonary artery to that lung has been visualized. Of course, the hypotension associated with excessive loss of blood is harmful. This may be prevented by careful dissection and avoidance of collateral vessels wherever possible and must be treated by the administration of plasma or whole blood during the operation.

Arrhythmia during operation (Table III). Twenty-one patients (4.2 per cent) died during anesthesia or operation. The deaths occurred at any time during this period and could not be correlated with any specific event, except in two instances in which a single pulmonary artery was occluded. Electrocardiograms taken on these 2 patients and on 5 others during the preterminal and terminal periods suggest that the depressant effect of anoxia was a major cause of death during operation. This is more fully discussed elsewhere (19).

An effort was made to correlate the preoperative oxygen saturation of the arterial blood and the exact anatomic defects with the incidence of death during this period. No direct correlation could be made (Table III). Arterial oxygen saturation of the 21 patients ranged from 7 to 72 per cent and averaged 38 per cent. This is slightly lower than the average of 54 per cent for 30 consecutive successful cases taken at random; the values ranged from 15 to 81 per cent. All 21 patients in this group were considerably incapacitated. Nonetheless, there were several patients with an apparently uncomplicated tetralogy of Fallot and a relatively high oxygen saturation who died during operation.

In order to evaluate more accurately the role of anoxia in the causation of bradycardia, we should have serial determinations of arterial oxygen saturation during operation. This has been done to a limited extent by the use of the oximeter, both here and elsewhere (1). Neural and chemical mechanisms may also be important, but at present the data are meager.

The prevention and treatment of arrhythmia during operation and anesthesia has been fully discussed in previous publications (2, 19). The most important precautionary measure is the maintenance of adequate systemic oxygenation as described. The judicious use of digitalis, cardiac stimulants and transfusions of whole blood has been effective.

In one of the two instances mentioned in which a single pulmonary artery was occluded, observations demonstrated a sign which may be pathognomonic of this uncommon condition. When the branches of the pulmonary artery were occluded distally, the proximal artery became tense, pulsations diminished, and the artery no longer collapsed in diastole. It was realized later that in the presence of a competent pulmonary valve, which is usually found, the pressure in the segment of artery isolated by distal occlusion will rise to approach the right ventricular systolic pressure when there is no outlet through a pulmonary artery to the other lung. This finding was also noted in a patient in whom a previous end-to-end anastomosis had been done on the opposite side with proximal ligation of the pulmonary artery to that lung. In the 2 fatal cases in patients without a left pulmonary artery the right pulmonary artery had been occluded for 3 minutes and 10 minutes respectively before any significant change was noted in the action of the heart. Although it is unwise to occlude the pulmonary artery for a long period as a test for adequacy of the contralateral pulmonary circulation, one may

TABLE III.—DEATH DURING OPERATION

Name No.	Age Sex	Incapacity	Oxygen saturation (Per cent)	Time of death	Anatomic diagnosis	Comments
J.P. 187	5 years F	Moderate	43	Opening chest	Pulmonary atresia	
N.Q. 207	2½ years M	Moderate	42	Opening chest	Pulmonary atresia	
M.B. 309	17 years F	Moderate	72	Opening chest	Valvular pulmonary stenosis. Patent foramen ovale	Unexplained death before chest opened
M.K. 126	7 years M	Moderate	40	Mediastinal dissection	Tetralogy	
I.S. 229	7 years M	Moderate	65	Mediastinal dissection	Tetralogy, single pulmonary artery	Clamp on single pulmonary artery
B.C. 248	4 years M	Moderate	36	Mediastinal dissection	Tetralogy with atresia	
G.B. 308	2 years F	Extreme	26	Mediastinal dissection	Single ventricle	
D.K. 19	5 years M	Extreme	41	During anastomosis	Tetralogy	
C.D. 96	8 years F	Moderate	29	During anastomosis	Tetralogy	
S.S. 361	2 yea s F	Moderate	36	During anastomosis	Truncus arteriosus, no pulmonary artery	
B.L. 373	8 years F	Extreme	34	During anastomosis	Tetralogy, single pulmonary artery	Clamp on single pulmonary artery
H.G. 403	26 years F	Extreme	38	During anastomosis	Pulmonary stenosis, tricuspid atresia	
S.S. 440	3 years F	Extreme		During anastomosis	Tetralogy	
K.M. 90	2½ mos. F	Extreme	17	After completion of anastomosis	Pulmonary atresia	
R.D. 125	4½ mos. F	Extreme	18	After completion of anastomosis	Pulmonary atresia	
P.N. 128	7 mos. M	Extreme	13	After completion of anastomosis	Truncus arteriosus, no pulmonary arteries	
D.B. 153	14 years M	Moderate	64	After completion of anastomosis	Valvular pulmonary stenosis. Single ventricle	Complete heart block, acute dilatation
C.H. 158	15 years M	Moderate	63	After completion of anastomosis	Tetralogy, anomalous venous return	
C.F. 161	23 mos. F	Extreme	7	After completion of anastomosis	Pulmonary atresia	
D.C. 172	8 years M	Extreme	46	After completion of anastomosis	No autopsy	
C.P. 490	1½ years F	Extreme	68	After completion of anastomosis	Tetralogy	

gain valuable information by observing the effect of a short period of distal occlusion.

Cardiac failure and pulmonary edema (Table IV). When the Blalock operation was first reported it was known from the work of Eppinger, Burwell, and Gross that a patent ductus arteriosus might increase the work of the heart by as much as 400 per cent. It was hoped and expected, however, that cardiac enlargement after operation would only be temporary in patients with an artificial ductus arteriosus and that cardiac failure would not be a frequent complication (4). Studies of cardiac output after operation on these patients have demonstrated, as was expected, a large increase in cardiac output (17). Nonetheless, it has been gratifying to learn how few of them show signs of cardiac failure due to this increased load on the heart. Probably an important element in the low incidence of cardiac failure is the increase in oxygen saturation of the blood in the aorta and coronary arteries which occurs simultaneously with the increase in the load on the heart.

TABLE IV.—CARDIAC FAILURE AND PULMONARY EDEMA

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
S.L. 9	10 mos. M	Moderate	Frequent spells. Digitalis last 3 months	Heart slightly large. Ankles puffy	19	RI, ES.	Bilateral effusion. Died after 24 hours	Tetralogy. Heart and liver large. Pulmonary edema
B.T. 35	6 years M	Mild	Occasional precordial pain	Heart slightly large, rotated to right	59	RI, ES.	Pleural effusion, liver large, digitalized 6th day. Died 24th day	Single ventricle. Bilateral pleural effusion. Chronic passive congestion
E.G. 48	3 years F	Moderate	Negative	Large heart	37	LC, EE.	Peripheral edema. Discharged on digitalis. Died 67 days	Transposition great vessels. No pulmonary stenosis. 1500 c.c. hydrothorax
C.R. 56	2 years F	Moderate	None	Wide cardiac base. Hydrocephalus	46	Large RI, ES.	Increased pulse rate and lung markings by x-ray. Digitalized. Died at 40 hours	Tetralogy with atresia. Pulmonary edema
J.K. 61	2 years F	Extreme	Spells of unconsciousness	Marked cardiac enlargement	68	RS, EE to branch to upper lobe. Lung edematous	Pulmonary edema. Died 1½ hours	Tetralogy. Marked stenosis
A.S. 87	9 mos. M	Moderate	Convulsions with spells	Left ventricle slightly large. Left axis deviation by EKG	47	RI, ES. Transient bradycardia	Murmur disappeared, cyanosis returned 14 days. Failure after 10 months. Died at 11 months	Pulmonary and tricuspid atresia. Chronic passive congestion
N.M. 219	8 years M	Moderate	Negative	Typical tetralogy	29	Large RS, ES.	Pulmonary edema at 12 hours. Died at 34 hours	Tetralogy with atresia. Mediastinal emphysema; pulmonary edema and hemorrhage
J.W. 343	8 mos. F	Moderate	Unconscious with spells	Typical tetralogy	28	Large RS, ES. Free pleural fluid	Pulmonary edema after 14 hours. Died at 24 hours	Tetralogy. Pulmonary edema and hemorrhage. Lobular pneumonia
D.M.F 353	8 years F	Moderate	Dry cough	Very large heart, both ventricles. Left axis deviation and right ventricular hypertrophy on EKG	57	Large RS, ES. Transient arrhythmia early	No increased failure until 3 months after operation. Then failed rapidly	Common atrioventricular ostium. Pulmonary stenosis
D.D. 359	3½ years F	Moderate	Negative	Heart slightly large, right and left	24	Large RS, ES.	Pulmonary edema 18 hours. Died 12 hours later	Tetralogy. Marked stenosis
P.K. 369	10 years M	Moderate	None	Heart of normal size. Situs inversus viscerum with levocardia. Increased hilar markings	56	LI, ES. Bradycardia once	Recurrent bilateral effusion and decompensation. Died at 7 months	Single auricle. Aorta from RV. Moderate pulmonary stenosis. Abnormal venous return
H.B. 384	3 mos. F	Mild	Negative	Typical tetralogy	42	Large RS, ES. Transient arrhythmia once	Increased secretions and pulmonary edema 3d day. Digitalis. Died 5th day	Tetralogy. Marked stenosis. Pulmonary edema
R.D. 386	3 years M	Moderate	Mentally slow. Fainting spells	Chronic right otitis. Full sized heart. Large head	19	Large RS, ES. Transient arrhythmia once	Large liver on 3d day. Diarrhea 17th day. Pulmonary edema following clysis	Transposition great vessels. Large heart. Cerebral softening
W.L. 432	10 mos. M	Extreme	Unconscious spells	Large right ventricle		Aortic pulmonary, side-to-side	Pulmonary edema after 4 hours. Digitalized. Died after 38 hours	Tetralogy. Extreme stenosis. Pulmonary edema and hemorrhage
J.B. 439	12 years M	Moderate	Negative	Large heart. Increased lung markings. Liver large, shrank on digitalis	63	RS, ES. Transient arrhythmia on opening chest	Rapid pleural effusion started 2d day. Liver large. Digitalis. Died 67 days	Transposition great vessels. No pulmonary stenosis. 1500 c.c. hydrothorax

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

Fifteen, or 3.0 per cent of the first 500 patients died with manifestations of pulmonary edema or of congestive heart failure. Nine of the 15 patients had a large heart preoperatively and 5 of these patients exhibited other signs of failure. This, of course, is not the case in the typical tetralogy of Fallot as a small heart is the usual finding.

In 13 of the 15 patients there was reason to think that the burden imposed on the heart by operation was greater than usual. These 13 patients had an unusually large anastomosis constructed by the use of either the innominate or carotid artery, a large opening in a side-to-side aortic pulmonary anastomosis, or in 5 cases an unusually large subclavian artery. Potts, Smith, and Gibson have advised limiting the size of the opening in the aorta to avoid too large a shunt of blood to the lungs when an aortic pulmonary anastomosis is performed. In a subclavian pulmonary anastomosis, on the other hand, the size of the subclavian artery usually prevents too large a shunt of blood. However, with the use of the innominate artery or an unusually large subclavian, an overwhelming burden may be placed on the heart.

In the 2 remaining patients there were unusual influences at work. J.K. (No. 61) had a large heart preoperatively with a cardiothoracic ratio of 0.58. Following an end-to-end anastomosis to a small artery not recognized as the branch to the upper lobe, generalized pulmonary edema promptly developed and she died 1½ hours after operation. The explanation for the decompensation in the other patient, J.B. (No. 439) was found at autopsy in a transposition of the great vessels which had not been previously suspected. He had a large heart with an interauricular septal defect but there was no pulmonary stenosis or interventricular septal defect. The increased load on an already overworked heart was manifested in the rapid development of hepatomegaly and pleural effusion.

Most of these patients either had a large heart or else had a large anastomosis created. The large heart should not be a contraindication to operation, nor should the size of the systemic artery alone determine what type of anastomosis one should make. An artificial ductus large enough to relieve the anoxemia without imposing too heavy a burden is ideally adapted to improve the pulmonary circulation. Hence nice surgical judgment is required to select the proper vessel for anastomosis when the subclavian artery is small or to constrict slightly the anastomotic lumen when the subclavian artery is unusually large. The preoperative size of the heart must be borne in mind in making this decision.

These patients were equally divided between those who had signs of generalized cardiac decompensation and those who showed signs primarily of pulmonary edema. In all patients of the latter group there was extreme or complete pulmonary stenosis. Since the diagnosis of extreme stenosis can be suspected from the pronounced incapacity and cyanosis of the patient, absence or faintness of the murmur, scant lung markings on fluoroscopy and evidence of increased collateral circulation at operation, one must be cautious of creating a large ductus in such instances. The patients in whom generalized cardiac decompensation developed include 3 with transposition of the great vessels, 1 with a single ventricle, 1 with tricuspid atresia and a functional single ventricle, 1 with a common atrioventricular ostium and a single coronary artery, and 1 patient with coronary occlusion. The last patient became decompensated while in the hospital and was found at autopsy 6 months later to have calcification of the coronary arteries with extensive areas of coagulation necrosis, chronic passive congestion, and generalized medial necrosis of the peripheral arteries. Only the last of these patients had extreme pulmonary stenosis.

Patients with an enlarged heart, previous evidence of cardiac failure, single ventricle, or tricuspid atresia, and others with pulmonary stenosis who show signs of variation from the typical tetralogy of Fallot should not be eliminated from consideration for surgical therapy since good results have been obtained in all these conditions. One must be aware of the increased risk, however, and must look for possibly remediable complications.

A case illustrative of benefit which may attend the production of a ductus arteriosus in an atypical case is that of W.B. (No. 234) men-

tioned previously among the deaths from cerebral damage. There was evidence of mild cardiac decompensation which was improving when he died a month after operation of an apparently spontaneous cerebrovascular accident. At autopsy there was seen an unsuspected transposition of the great vessels with a small interventricular septal defect but no overriding aorta, and pulmonary stenosis. The improvement in this patient and in many other cases of pulmonary stenosis without the typical configuration of the tetralogy of Fallot demonstrates the wide range of usefulness of the operation. Theoretically any patient should benefit who has a diminished blood supply to the lungs as a result of pulmonary stenosis and a right to left intracardiac shunt of venous blood into the systemic circulation. This statement has been borne out in actual practice, although many elements affect the ultimate prognosis.

The treatment which we employ for cardiac failure developing postoperatively does not differ from that in common use. Rest in bed, the administration of oxygen, digitalis, and diuretics, a low salt diet, and possibly venesection are usually adequate to restore cardiac compensation during the early period of adjustment. The development of pulmonary edema is an entirely different matter, however, and in no instance in which there was more than minimal edema has the patient recovered. Consequently, we endeavor to prevent this complication whenever possible. When one anticipates this condition the fluid intake should be limited to 40 to 60 cubic centimeters per kilogram of body weight per day in children and less in adults. A striking increase in pulmonary vascular markings as seen in the portable roentgenogram on the night of operation should make one anticipate the appearance of clinically obvious edema. Any patient who shows signs of cardiac decompensation before operation must be digitalized. Patients who are submitted to an end-to-end anastomosis for reasons other than the presence of a very small pulmonary artery, —for example, a short systemic or pulmonary artery—probably should lie on the side not operated upon in the early postoperative period to prevent venous congestion.

Hemorrhage (Table V). In 7 patients massive bleeding was the primary cause of death. As one of the means of compensating for decreased pulmonary circulation these patients have many dilated and engorged vessels in the chest wall and mediastinum. These are often troublesome during the dissection of the mediastinal structures and probably are the main site of postoperative bleeding. Because of a low blood flow the vessels on the lung may stop bleeding during the operation, only to open again following completion of the anastomosis and the shunting of an increased volume of blood to the lungs. In few cases is there any bleeding from the anastomosis, and in only 1 case has there been proof that this was the site of hemorrhage. In this patient, B.B. (No. 417), the mediastinum was dry when the chest was closed. When signs of persistent intrathoracic bleeding appeared, a secondary thoracotomy was performed, revealing blood spurting from the anastomosis. In the only other patient who was re-explored, the bleeding was coming from the chest wall; the anastomosis was intact.

The preoperative routine has not included studies on bleeding and clotting; hence such data were not obtained in any of these patients. B.B. (No. 417) had great prolongation of bleeding time, clotting time, and prothrombin time after re-exploration, but at that time she had received 4,000 cubic centimeters of blood, more than enough to replace her blood volume completely. The effect of this much blood on the bleeding and clotting mechanisms is difficult to evaluate. Almost all of the patients studied have shown a slight prolongation of the prothrombin time before operation. The cause of this is obscure, but it would appear to be beneficial by counteracting the thrombosing effect of the polycythemia.

Two of the patients gave a history of unusual bleeding. One had bled from her tonsils spontaneously without evidence of infection, and the other had experienced 2 recent hemoptyses. In 3 patients dying of hemorrhage, anticoagulant therapy was instituted during the postoperative course. P.Mc.M. (No. 42) was given dicoumarol on her second and third postoperative days. Her prothrombin time remained normal. On the fifth post-

TABLE V.—HEMORRHAGE

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
P.M. 42	11 years F	Mild	Negative	Typical tetralogy	75	RS, ES.	Did well. Dicumarol 2d and 3d day without change in prothrombin time. On 5th day coughed up 200 c.c. blood, died	Tetralogy. Bleeding point not seen
S.D. 202	17 years M	Extreme	Recent transient blindness	Slightly large heart. Scoliosis	49	RC, ES. Bradycardia 3 times, pupils dilated before carotid tied	Hypotensive early. Hemiplegia 1st day. Heparin. Known fluid in chest but heparin continued. Died with hypotension	Tetralogy. Massive hemothorax. Thrombus in carotid. Hemorrhage in cortex
V.B. 210	14 years F	Extreme	Negative	Slightly full pulmonary conus. Underweight	75	RS, ES with vein graft. Much bleeding. Heparin given at operation	Hypotensive on ward. Pulmonary edema after vigorous replacement therapy	None. 2,500 c.c. of blood aspirated post mortem
R.V. 261	14 years M	Moderate	3 convulsive attacks at 2 years. Mentally slow	Dextrorotation. Increased lung markings	70	RC, ES. Very bloody.	3,250 c.c. blood aspirated from chest, replaced by transfusions	Functional single ventricle. Pulmonary atresia
J.H. 278	17 years M	Moderate	2 recent hemoptyses	Typical tetralogy. Scattered petechiae	80	LS, ES. Slight ooze controlled with gelfoam	Satisfactory for 5–6 hours. Then hypotension. BP restored with blood. Re-explored, unable to stop ooze	Tetralogy. Hemothorax
R.L.W. 336	11 years M	Moderate	Meningitis 6 months before	Typical tetralogy	57	RS, ES. Bradycardia early, paroxysmal tachycardia at end	Given 2,500 c.c. plasma and blood. Acute shock after 4 hours, died 2 hours later	Tetralogy. Marked stenosis. Hemothorax. Small intimal tear
B.B. 417	4 years F	Moderate	Negative	Typical tetralogy. Tonsils bled easily; no evidence of infection	57	RS, ES. Retroesophageal subclavian	Blood pressure fell as anastomosis opened. Hemothorax aspirated on ward. Re-explored. Bleeding from anastomosis in spurts. After 4L of blood, clotting time 40 minutes; prothrombin content 25 per cent of normal	Tetralogy. Pronounced stenosis. Petechiae in all organs

*See Table VI for explanation of letters.

operative day, after having seemed well several minutes before, she suddenly coughed up about 200 cubic centimeters of frothy blood and rapidly died. Since that time anticoagulants have been used only for specific postoperative complications; namely, thrombosis of the anastomosis, or a possible cerebral thrombosis. One of the other patients to receive anticoagulants, V.B. (No. 210), had a long and difficult operative procedure in which a vein graft was used. Heparin was administered on the operating table. She died 5 hours later in spite of massive replacement therapy. Two thousand five hundred cubic centimeters of blood was aspirated from her chest *post mortem*. If heparin is to be used we believe it should not be started for 6 to 8 hours after operation. The third patient bled profusely into his chest on the day of operation. The following morning there was left hemiplegia and heparin was given by the continuous intravenous method. With improvement in the cerebral signs, administration of heparin was stopped the following day but was started again 24 hours later when the cerebral signs reappeared. Repeated attempts at aspiration of the chest were of no avail, and he died on the sixth postoperative day with 4,250 cubic centimeters of partly clotted blood in the pleural cavity on the side operated upon.

Thrombosis of the anastomosis (Table VI). In 5 instances thrombosis of the anastomosis seemed to be the most important cause of death. These patients either failed to get the expected early benefit from operation, or improved for a time only to become rapidly worse with disappearance of the continuous murmur. Patients placed in other groups in this report also had varying degrees of thrombosis of the anastomosis as seen at autopsy, but other causes seemed more important in their fatal course.

TABLE VI.—THROMBOSIS OF ANASTOMOSIS

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
G.G. 95	5 years M	Extreme	Spells of unconsciousness	Large heart, full conus	47	LS, EE. Very small pulmonary artery	Satisfactory until 18th day. Became cyanotic, murmur disappeared. Died on 19th day	Cor biloculare. Pulmonary atresia. Thrombosis of anastomosis
D.O. 103	7 years F	Moderate	Transient left hemiparesis in hospital	Small heart	50	RI, EE. Tiny pulmonary artery	Satisfactory for 36 hours, then pallar, tachypnea. Very cyanotic	Not done
S.J. 137	16 years F	Extreme	CVA at 6 years. Oral hemorrhage 12 years	Large heart. Scoliosis	57	LS, ES. Cyanotic during dissection. Hypotensive 40 minutes, difficult anastomosis	Remained hypotensive. Poor response. Died 12 hours later	Tetralogy. Thrombosis of anastomosis. Suture caught posterior wall
R.A.B. 184	22 mos. F	Extreme	Frequent spells	Typical tetralogy	21	RI, ES. Difficult anesthesia	Early course satisfactory. Hemiparesis 12 hours	Tetralogy. Thrombosis of anastomosis
C.R. 266	2 years M	Moderate	Mentally slow	Large head. Typical tetralogy	34	Large RS, distal to branches, ES. Bradycardia once	Improved for 4 hours. Color, respirations, pulse worsened. No murmur	Tetralogy. Anastomosis thrombosed into pulmonary artery

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

Several factors are important in relation to thrombosis of the anastomosis. A perplexing problem is the extremely small pulmonary artery which is occasionally encountered. In such instances even an end-to-end anastomosis is difficult because of the disparity in size between the pulmonary and systemic arteries, and such anastomoses are notoriously prone to thrombose. Care must be taken in all cases to avoid suturing the posterior wall of the vessels when completing the anastomosis anteriorly. If additional sutures are needed after completion of the anastomosis, they are best placed with the occluding devices removed and the arteries distended.

In patients with a large, short subclavian artery one is often tempted to use the subclavian artery distal to its first 3 or 4 branches. This is especially true where all branches arise over a short distance. Such a vessel should be used only when a long and large segment of artery can be obtained distal to the branches, for the presence of thrombus in the adjacent branches may predispose to thrombosis of the anastomosis, as occurred in C.R. (No. 266).

Many of the fatal cases had small thrombi at the suture line, but these constricted the lumen very little and could scarcely affect the flow significantly in the presence of the large pressure gradient between the systemic and pulmonary arteries. One need have little fear of an occluding thrombosis if a satisfactory anastomosis is obtained. Because of this observation and because of the fatal hemorrhage described above during dicumarol therapy, the prophylactic use of anticoagulants has been abandoned.

Respiratory complications (Table VII). It is a favorable commentary on present day thoracic surgery with its improved anesthesia and prophylactic use of antibiotics, that only 4 patients died as a result of respiratory complications. In 2 of these patients tension pneumothorax developed, a complication which has been infrequent and of no consequence since these deaths occurred early in the series. E.S. (No. 1) seemed particularly susceptible to pneumothorax, as this condition developed after the first procedure and again after an operation on the other side 10 months later. In the 2 other patients a refractory pneumonia appeared in spite of the penicillin given prophylactically after operation as to all patients. One of these patients, J.B. (No. 274), was found to have at autopsy a clinically unsuspected transposition of the great vessels without pulmonary stenosis or an overriding aorta. After operation he had a great deal of tracheo-

TABLE VII.—RESPIRATORY COMPLICATIONS

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
E.S. 1	2 years F	Marked	Improved after previous operation then worsened	Heart slightly large	16.2	RI, ES. (Previous LC)	Pneumothorax. Cyanosis continued	Not done
L.M. 39	3 years M	Moderate	Spells of unconsciousness	Typical tetralogy	24	LI, ES.	Tension pneumothorax. Later pulmonary edema	Tetralogy. Perforation of pleura and left lung
J.B. 274	4 years M	Marked	Two hemiplegias	Full conus. Increased lung markings	30	RS, ES. Large pulmonary artery. Pressure 435 mm.	Much tracheobronchial mucus, pneumonia 3d day. Tachycardia	Transposition of great vessels. No pulmonary stenosis. Encephalomalacia
J.C. 433	22 years M	Moderate	Left hemiplegia at 2 years of age	Heart slightly large. No concavity of pulmonary conus	70	RC, ES. None	Early stupor improved on heparin. Pneumonia 7th day. Died on 8th	Tetralogy

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

bronchial mucus requiring frequent aspiration. We are unable to state whether the excessive mucus represented an infectious tracheobronchitis from the start, or whether the dynamics of the altered pulmonary circulation were such that secretions were increased in the respiratory tract. The absence of fever early in his postoperative course would support the latter belief, as would the somewhat similar course and anatomical findings on R.D. (No. 386), Table IV, who had a large amount of mucus but did not have pneumonia.

Shock (Table VIII). Two patients did not reach any degree of cardiovascular stability after operation and died as a result of operative shock. No anastomosis was performed in either case. In 1 of these the operation was terminated because no pulmonary artery could be found among the multitude of collateral vessels. At autopsy it occupied an anomalous position posterior and inferior to the bronchus. In the other patient there was considerable bleeding and the procedure was abandoned when the heart action became poor during the unsuccessful exploration of the upper mediastinum for the subclavian artery. At autopsy this vessel was found to course behind the esophagus in reaching its destination in the apex of the chest.

Shock was undoubtedly an important contributing cause in many other patients who died early in the postoperative period. With further improvement in the care of patients under anesthesia and during exploration of the mediastinum, the prominence of this cause of death should lessen.

Miscellaneous causes (Table IX). This group includes 23 patients who died of miscellaneous causes. In some, death was unrelated to the operation; some died outside of

TABLE VIII.—SHOCK

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
H.E. 28	4 years M	Extreme	Negative	Typical tetralogy Extremely ill	27	Pulmonary artery not found	Responded poorly, hypotension, tachycardia	Tetralogy with atresia. Right pulmonary artery posterior and inferior to bronchus. Several pulmonary veins entered superior vena cava
H.G. 66	20 years F	Extreme	Fainting spells	Large heart	89	No anastomosis. Heart action poor. Hypotensive	Hypotension continued, no response	Tetralogy. Hemothorax. Early coronary sclerosis

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

TABLE IX.—MISCELLANEOUS CAUSES

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
P.C. 5	4 years F	Moderate	Taking digitalis	Typical tetralogy	17	RC, ES. Anesthesia difficult	Unsatisfactory without specific trouble. Began having spells. Died with spell 9 months after operation	Not done
S.C. 14	10 mos. M	Moderate	Opisthotonos with spells	Large globular heart. Undernourished	28	RI, ES.	Cerebral signs which cleared. Discharged slightly improved. Died after 10 months	Thrombosis of longitudinal sinus. Right encephalomalacia
R.B. 36	11 years M	Extreme	3 years in Japanese prison camp. Unconscious with spells	Large heart. Gallop rhythm	46	RS, ES. Large subclavian	Slowly failed. Died after 7 days	Tetralogy. Chronic passive congestion. Acute and chronic bronchitis
D. McP. 37	7 years M	Mild	Negative	Typical tetralogy	88	RC, ES.	Benign and satisfactory course. Died 2 years after operation of acute myelogenous leucemia	Typical tetralogy
A.M.P 57	10 mos. F	Moderate	Negative	Slightly large heart	35	Large RS, ES. Carotid divided	Intermittent unexplained fever. Encephalogram showed marked cortical atrophy. Died 3½ months after operation with intercurrent infection	Not done
E.E. 83	8 years M	Extreme	Negative	Typical tetralogy	39	RC, ES. Bradycardia early	Frothy pink sputum when anastomosis opened. Died 30 minutes later	Tetralogy with atresia. Anastomosis done to superior pulmonary vein. Wet infarct, right upper lobe
M.A. M. 85	2½ years M	Extreme	Negative	Heart enlarged to right	11	RI, ES.	Early course satisfactory. Died 20 hours postoperatively after small dose morphine	Tricuspid atresia. Patent ductus. Left lung collapsed, atelectasis
B.F. 114	11 years F	Mild	Negative	Typical tetralogy	60	LS, ES. Pressure in pulmonary vessel, 125 mm. Pericardium opened to identify vessel	Sudden pulmonary edema after 4 hours	Tetralogy. Pronounced stenosis. Lung edematous. Anastomosis to superior pulmonary vein
G.T. 148	15 mos. F	Extreme	Opisthotonos with spells	Typical tetralogy	13	Large RS, ES.	Murmur not heard. Showed signs of cerebral damage. Died 10 months later in a spell	Not done
L.R. 173	8 years M	Moderate	Negative	Typical tetralogy	57	No anastomosis. Pulmonary pressure more than 1150 mm.	Tachycardia. Restless 5th day was doing well, screamed and died	Transposition great vessels
P.D. 177	5 years F	Mild	Negative	Typical tetralogy		RS, ES.	Benign. Died on boat to Trinidad unattended medically. Recent tooth extraction	Not done

*Letters refer to the use of right or left subclavian, carotid, or innominate artery, end-to-side or end-to-end in a systemic pulmonary arterial anastomosis.

TABLE IX.—MISCELLANEOUS CAUSES—Continued

Name No.	Age Sex	Incapacity	Special history	Clinical findings	Oxygen saturation (Per cent)	Operation*	Course	Autopsy
D.B. 211	7 years M	Moderate	Negative	Slightly large heart	59	RS, ES.	Benign course. Improved. Died after nausea, vomiting, bilirubinuria, fever, slight jaundice, delirium. No cyanosis	Not done
R.C. 212	3 years M	Moderate	Feeding problem. 3 transient paralyses last 6 months	Typical tetralogy	13	Large RS, ES.	Benign course. Improved. Pneumonia 6 months later with fatal relapse	Not done
A.S. 246	21 years F	Moderate	Negative	Typical adult tetralogy	75	LS, ES.	Not improved. Died 18 months later of hemorrhage after operation on other side at another hospital	Typical tetralogy
J.C. 275	30 mos. M	Extreme	Feeding problem. Convulsions with spells	Typical x-ray. Complete heart block. Occasionally gasp in respiration	41	RS, ES. Arrhythmia unchanged	Seemed better until 12 hours, then suddenly pulseless	Tetralogy. Pulmonary edema. Small left ventricle and great vessels rotated
R.M. 291	19 mos. M	Extreme	Recent facial twitchings	Slightly large heart. Fontanel patent 3 cm. Slight right facial palsy, right extremities spastic	20	LS, ES.	Improved mentally and physically. Saturation 63%. Died 3½ months later	Cerebral infarction
R.A. 320	22 years M	Moderate	Negative	Typical tetralogy small	82	RS, ES. Bradycardia early	Blood pressure 60–75. Good pulse and skin temperature. Sudden collapse after 31 hours. 400 c.c. thoracentesis	Tetralogy 400 c.c. blood each chest. Chronic passive congestion. Lungs edematous
C.G. 344	3 years M	Moderate	Negative	Typical tetralogy	36	RS, ES.	Tracheobronchitis and decompensation early both transient. Fatal meningitis after returning to France	No report
J.S. 355	5 years F	Moderate	Negative	Typical tetralogy	33	LS, ES.	Hypotension, responded poorly. Sudden death 9 hours after operation	Typical tetralogy
R.S. 415	7 years M	Mild	Negative	Typical tetralogy	63	RS, ES.	Uncomplicated course, died suddenly 10 mos. later without explanation	Typical tetralogy
N.P. 441	20 years F	Moderate	Renal shutdown 5 years ago with sulfonamide	Typical tetralogy	61	RS, ES. Double aortic arch	Benign convalescence. Died suddenly on 5th day after getting out of bed	Tetralogy. Ball thrombus left ventricle. Two infarcts left lung
C.N. 479	16 years F	Moderate	Negative	Typical tetralogy	65	RS, ES. Pericardium opened inadvertently, not closed	Slight decompensation on arising. Sudden death PO 18 during pericardial tap	Tetralogy. No cause of death seen
J.L. 495	4 years M	Moderate	Hemiplegia at 6 weeks. Many epistaxes	Typical tetralogy	56	RS, ES. Convulsions during anastomosis and during closure	Did well for 10 hours then gasped, struggled and died	Tetralogy

TABLE X.—CARDIAC FINDINGS AT AUTOPSY

	Number of patients
Tetralogy of Fallot	55
Tricuspid atresia and pulmonary atresia or stenosis	4
Atypical*	15
Transposition of the great vessels	6
Pulmonary artery to one lung only	3
Incidental disease with typical tetralogy†	4
No autopsy	12
	99

*This includes 5 patients with single ventricle, 3 with atrioventricularis communis, 3 without an overriding aorta, 2 with complete rotation of the great vessels and heart chambers, 1 with Cooley's anemia, and 1 with "pseudo-truncus arteriosus." All had pulmonary stenosis and a right to left intracardiac shunt.

†One instance each of meningitis, leucemia, pneumonia, and coronary occlusion.

the hospital with only incomplete data available; and in some the cause of death was obscure. On 2 occasions the systemic artery was anastomosed to the superior pulmonary vein by mistake. In the second of these patients the vessel in question was strongly suspected of being the vein, but the pressure measured directly was 125 millimeters of saline. No pulmonary artery could be found at operation or later at autopsy. Both of these patients had wet infarcts of the upper pulmonary lobe on the side operated upon. When there are many collateral vessels, especially in patients with anomalous vascular patterns or rotation of the heart, one may readily mistake the superior pulmonary vein for the pulmonary artery. If dissection is carried far enough 2 important differentiating features will be apparent: (1) The vein follows a more oblique course in contrast to the transversely lying right or left pulmonary artery, and (2) tributaries of the vein are more numerous in or adjacent to the hilum than are branches of the artery. Measurement of pressure or estimation of the color of blood in the vessel is of little value with the open thorax and collapsed lung.

One patient, R.B. (No. 36), had spent 3 years in a Japanese prison camp and was extremely malnourished and severely incapacitated. He died on the seventh postoperative day after slowly failing in strength. His death was attributed to extreme and prolonged malnutrition. D.M.P. (No. 37), obtained an excellent operative result but died 2½ years later of acute leucemia. C.G. (No. 344) had a satisfactory course in the hospital but suffered a fatal meningitis on returning to his home in France. One patient, S.C. (No. 14), who died elsewhere, was found to have thrombosis of the longitudinal sinus and encephalomalacia, and another, R.M. (No. 291), a cerebral infarct. These occurred respectively 10 and 3½ months after operation. Both of these patients were under 2 years of age and probably did not get sufficient benefit from the operation to relieve cyanosis and polycythemia. N.P. (No. 441) died suddenly on her fifteenth postoperative day, after a previously uneventful course. Autopsy disclosed a ball thrombus in the left ventricle which presumably caused her death by momentarily plugging the interventricular septal defect. C.N. (No. 479) died during a pericardial aspiration, probably of ventricular fibrillation. Three patients, R.A. (No. 320), J.L. (No. 495), and J.C. (No. 275), died very suddenly within the first 2 days after operation and without prior evidence of difficulty. The last of these had a complete heart block before operation which may have been the cause of his death. The first of these patients had been studied by Vandam, Bing, and Gray and a low volume of systemic blood flow had been determined by cardiac catheterization. It was suggested by them that a further reduction in the volume of systemic flow by the creation of a ductus arteriosus may have been responsible for the postoperative hypotension and death. A hemothorax of moderate size undoubtedly added to the diminution in cardiac output. R.C. (No. 212) made some improvement but died 5 months later of pneumonia. G.T. (No. 148) died 10 months after a stormy hospital course in which the continuous murmur disappeared and pronounced cerebral signs appeared. The cyanosis and incapacity continued unabated. A.M.P. (No. 57) died 3½ months after operation. She had a stormy early course with little improvement and several intercurrent infections. She failed gradually and showed signs of cardiac decompensation during the last few days. A.S. (No. 246) was not improved by a small subclavian anastomosis. She died of hemorrhage following a second operation on the opposite side at another hospital.

In the 7 remaining patients the cause of death remains obscure in spite of autopsies on

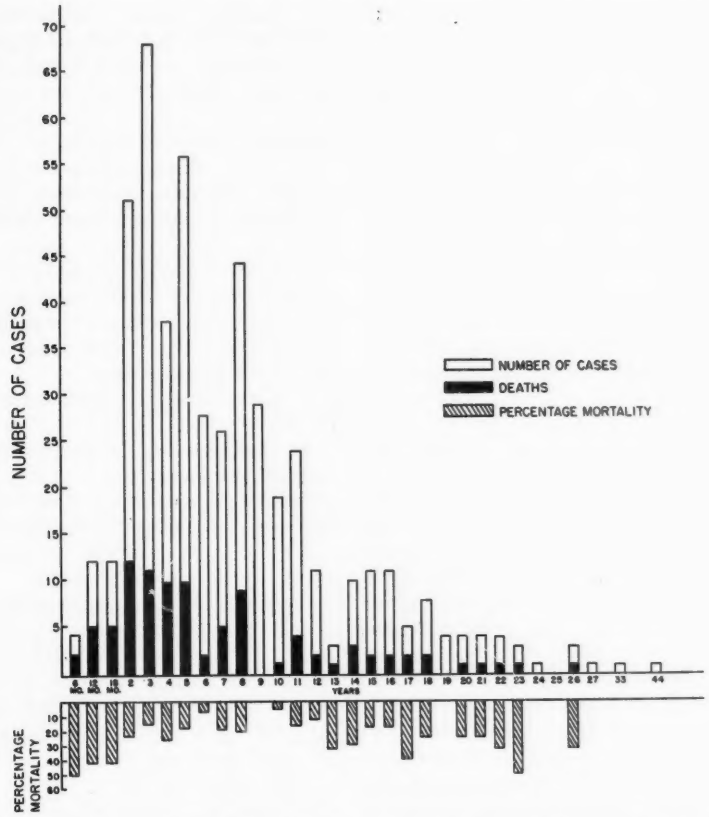

Fig. 1. The most favorable age for operation, based on mortality rate is between 2 and 12 years.

5 of them. In connection with 1 of the patients on whom an autopsy was not performed the possibility of subacute bacterial endocarditis was mentioned without proof (P.D., No. 177).

DISCUSSION

The seemingly forbidding mortality rate of 1 patient in 5 in this series must be balanced against the generally poor prognosis of patients with congenital heart disease and cyanosis. No attempt has been made to calculate a "corrected" mortality rate. Many of the patients operated upon were known to be atypical, and some were inaccurately diagnosed (Table X). Four patients died of disease unrelated to their congenital cyanotic heart disease. No patient has been denied operation because of the severity of his illness, and several have died while in the hospital awaiting operation. In 358 patients of the first 500 cases who survived the preferred operation, namely a subclavian pulmonary end-to-side anastomosis, the mortality rate was 12.6 per cent.

As in most surgical conditions, a patient who has a poor prognosis without operation presents a greater operative risk. With the extensive use of cardiac catheterizations and angiocardiography, the indications for operation have been broadened to include patients who were thought inoperable when experience with this procedure was small. This is one of the elements which prevented a significant

lowering of the mortality rate in the last half of the series. Regardless of the complicating features in the atypical cases, parents and adult patients ask that the operation be attempted even when informed of the added risk.

From Figure 1 it can be seen that the preferred age for operation, judging from the mortality rate, is between 2 and 12 years inclusive. Prior to this period compensatory mechanisms are still developing and the operative procedure is more difficult because of small structures. Beyond the age of 12 the distance between the systemic and pulmonary arteries is likely to be out of proportion to the length of the subclavian artery and one is more often required to use the carotid artery or to do an end-to-end anastomosis. Because of this, in tall or older patients it is advisable to enter the chest on the side of the aortic arch and use the subclavian branch of the aorta or do an aortic pulmonary side-to-side anastomosis. The carotid or innominate artery is now rarely used. "Aging" seems to occur more rapidly than usual in the vessels of these patients and arteriosclerotic plaques are not uncommon in older patients.

SUMMARY

1. Of the first 500 patients operated on for congenital heart disease and cyanosis, 99 are dead at the time of writing, giving a mortality rate of 19.8 per cent. This includes deaths from all causes. In 4 patients incidental disease was the cause of death and in 6 a transposition of the great vessels was not diagnosed before death. In the group of 358 patients in whom the preferred operation was done, namely a subclavian pulmonary end-to-side anastomosis, the mortality rate was 12.6 per cent.

2. Twenty-two (4.4 per cent) of the patients died as a result of cerebral complications. Contributing factors to this are severe arrhythmia or anoxia at the time of operation, prior damage to the central nervous system, and the use of a carotid or the innominate artery in the anastomosis. The carotid or innominate artery is now rarely used.

3. Cardiac failure and pulmonary edema accounted for 15 deaths, or 3 per cent of the 500 patients. In most instances these were associated with preoperative cardiac enlargement or the creation of an unusually large artificial ductus arteriosus.

4. Hemorrhage was responsible for 7 deaths. It is felt that the main bleeding was from the collateral vessels and not from the anastomosis.

5. Thrombosis of the anastomosis is a rare complication (5 cases) and for this reason anticoagulants are not used prophylactically.

6. Respiratory complications were responsible for only 4 deaths.

7. Two deaths resulted from operative shock.

8. Twenty-three patients died from miscellaneous causes.

Suggestions are made which should aid in reducing the number of deaths in the future.

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ARTERIAL ANASTOMOSIS IN EXPERIMENTAL ARTERIAL INJURY

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IN this communication we wish to report the results of studies designed to evaluate in a quantitative manner the importance of arterial anastomosis in the problem of salvaging extremities that have sustained extensive injury with severance of their main arteries. The work to be presented is largely concerned with the establishment of a base line for a series of studies on the whole subject of arterial injuries. The first experiments to be reported herein have been done in order to establish the prognosis of arterial anastomosis under critical conditions. Several techniques of arterial anastomosis have been used. The execution of a good anastomosis is only one of the many requirements needed for a successful result in the whole operation of restoring circulation to a limb acutely deprived of blood. Other factors equally or even more important in salvaging limbs with arterial injury include the length of time that ischemia has existed before reparative surgery can be undertaken, the severity of the local injury and the coexistence of fractures. Before these data on arterial anastomosis are presented a brief summary of the experience obtained in the management of vascular wounds during World War II may be profitably reviewed since this experience formed the background for the work in our laboratory on this subject.

ARTERIAL INJURIES IN WORLD WAR II

Military surgery is primarily concerned with saving life. Abdominal and chest wounds may be found in patients with arterial wounds. Arrest of hemorrhage and repair of the abdominal and chest injuries demand attention first, and definitive arterial surgery may not be practicable. Nevertheless, early reparative vascular surgery was done in a substantial number of war wounded and should be possible more frequently in civilian practice.

While much progress was made in saving life and in the care of patients with vascular wounds, it was generally conceded by surgeons working in the forward areas that the record for saving ischemic extremities was poor (7, 22). The survival rate of lower extremities with severed major arteries was low not only when ligation of the vessels alone was performed but also when anastomosis was carried out (24). It was unfortunate that there had been no previous large experience with early definitive treatment of acute interruptions of major extremity vessels in World War I or in civilian practice upon which surgeons could have drawn. Very few immediate anastomoses were performed on soldiers with arterial injuries in World War I (17); late operations for the control of secondary hemorrhage and traumatic aneurysm comprised the major field of vascular surgery at this time (18). The number of such injuries among the civilian population is small (15). No one surgeon had had sufficient experience upon which to offer a plan for the overall management of these injuries at the beginning of World War II. It was perhaps equally unfortunate that the experience used as a guide for treatment was taken from our knowledge obtained in the management of arterial insufficiency as it is seen among patients with chronic occlusive vascular disease in civilian practice. Most of the early thinking and action was directed toward the use of measures designed to improve collateral circulation. Surgeons were preoccupied with the sympathetic nervous system's role in influencing the blood supply to the distal extremity. Too great an expectation was held for adjunctive therapy and particularly for the practice of chemical section of the lumbar sympathetic ganglia. In the

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severely wounded leg there is more often than not a destruction of collateral routes as well as of the major channel. Moreover, in most cases it is extremely doubtful that the small adjunctive vessels remaining after major artery severance can deliver sufficient blood to sustain life in the distal leg of young and vigorous individuals. Delay in attempting anastomoses of main arterial trunks resulted in some measure from a lack of appreciation of its necessity, although it is true that many patients were received too late to hope that restorative surgery might be done. In addition, material in the *Military Surgical Manuals* of the National Research Council indicated that a high incidence of leg survival might be expected after ligation of the femoral and popliteal arteries (19). This was a misleading prediction, and the experience cited was quite evidently taken from material other than the immediate results in vascular injuries of warfare. Extremity survival after arterial ligation performed on patients whose collateral routes had been developed by long-standing insufficiency is not at all comparable with that observed in patients with acute arterial interruption.

It was found that arterial wounds of the lower extremity were accompanied by a higher incidence of gangrene than in the arm. In the arm, fortunately, better collateral routes and adjunctive vessels are present for carrying blood distally after brachial artery interruption than exist in the leg when the popliteal artery is severed. It was a dismaying observation to find a 77 to 82 per cent amputation rate among wounded soldiers with femoral or popliteal artery injury who had been treated by ligation and supportive measures (24). Credit should be given to Blakemore for advocating early in World War II that arterial anastomosis be the method of choice, whenever it could be done, in preference to ligation although it remained for experience to prove the poor results of arterial ligation which were obtained even when all available adjunctive measures, including interruption of the sympathetic nerve supply, were used.

Although they were not as good as might be expected, the results in those cases in which some type of anastomosis was performed proved to be somewhat better than those obtained in patients who were subjected to ligation. Statistics on reparative surgery for vascular wounds in World War II show some variation in the reports of several authors although no one obtained strikingly good results (2, 7, 13, 14, 22, 24, 25, 26, 29). The three methods for reuniting arteries most frequently used were: end-to-end suture anastomosis, the Blakemore-Lord nonsuture vein graft, and tube prostheses of glass and plastic materials. A lower incidence of gangrene following suture repair was reported in the literature, but its superiority was not certainly established since the data in many instances have included the repair of lacerated as well as completely divided vessels. The problem of joining a completely interrupted artery with some loss of its substance is quite a different one from suture of a partial laceration. No single method of anastomosis could serve each case and circumstance. Not infrequently tension would not allow of end-to-end suture in the extensive arterial wounds and some scheme for bridging arterial defects was usually needed.

A perusal of the literature on arterial anastomosis in war injuries involving major arteries leads to the conclusion that unanimity of opinion on the indications for its employment was not reached. MacFee summarized the situation in his statement that a satisfactory method for restoring the function of the artery severed by a high velocity missile is yet to be developed. Nevertheless, occasional successes in small series of cases in which anastomosis or suture repair was performed early have been reported (3). The reasons for failure after arterial anastomoses could not be explained adequately in all instances. The variability of conditions in all series of reports was enormous as might be expected among battle casualties. In addition, it was true that a properly made, well functioning anastomosis failed to deliver blood to the distal extremity in cases that appeared favorable. In case of long delay between injury and definitive surgery it is quite possible that thrombosis in the smaller peripheral vessels had occurred. Patients with arterial injuries demand early evacuation and prompt surgical attention similar to the priority setup given patients with abdominal and thoracic wounds.

EXPERIMENTAL METHOD

The experiments to be reported have been designed to answer the following questions. What is the expectation for the survival of an ischemic extremity upon which immediate reparative arterial surgery has been done under the conditions of a clean wound? Secondly, how does the efficiency of the various methods currently used for reuniting severed arteries compare? In order to answer these questions it was necessary to make an animal preparation in which the blood supply to the distal extremity depended upon a single artery. Unfortunately, no animals are available for experimental purposes in which a high incidence of gangrene results from femoral artery ligation (3, 20). In order to be comparable to the situation which obtains in human subjects gangrene in an experimental preparation should follow femoral artery ligation in approximately 75 per cent of cases in which acute interruption has been done. Some alteration of the blood supply to the dog's leg seemed the best approach for obtaining a suitable test animal.

Preliminary experimental preparation. It was hoped that preliminary ligation of multiple vessels might be effective in making a single arterial channel for the hind limb of the dog from the aorta through the external iliac and femoral arteries. With these vessels and their branches occluded, it was expected that gangrene might occur in a predictable majority of cases upon subsequent ligation of the femoral pathway. The advantage of such a control preparation with a normally functioning limb as vulnerable as the human subject to femoral artery interruption would have been great. Forty-eight animals were subjected to the ligation of as many as 120 arteries and their branches which, by means of many dissections and arteriograms, had been found to contribute directly or indirectly as potential collateral pathways to the blood supply of one rear extremity. Approximately 20 hours of operating time in as many as 5 stages through 4 or 5 incisions upon or adjacent to the affected extremity were completed in single animals. Following the subsequent ligation of the femoral artery from periods of immediately to as long as 7 days after the last preliminary ligations the overall incidence of gangrene in 35 dogs surviving these operations was only 39 per cent. This figure included several dogs in which gas gangrene developed. When contamination was better controlled in such preparations the incidence of gangrene fell to approximately 20 per cent. This incidence of gangrene resulting from femoral artery ligation by this method was far too small for the critical preparation needed.

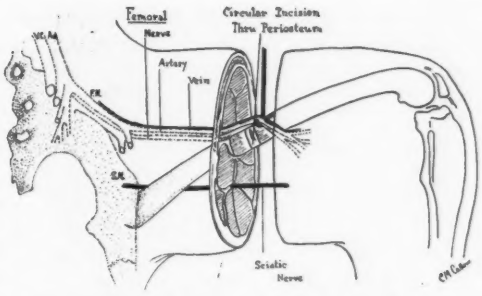

Fig. 1. Diagram of transected hind limb showing the structures left intact (after Reichert).

Final experimental preparation. A partially amputated and reimplanted limb appeared to be the only means of obtaining a preparation in which the collateral vessels could be definitely occluded for a known period of time. Halsted, Hoepfner, Carrel and Guthrie (6), and Reichert have utilized such a preparation for other purposes. With minor modifications indicated in the description of the technique for the operation given later, it was found to be a highly critical method for testing the integrity of a single artery anastomosis.

Large dogs weighing from 40 to 50 pounds were used. Nembutal given intravenously and supplemented by ether was employed for anesthesia. The hind limb of the dog was transected at the junction of the middle and upper thirds, with preservation of the femur, femoral and sciatic nerves, and the femoral artery and vein (Fig. 1). The preserved structures were carefully inspected for the presence of accompanying blood vessels which were ligated when found. Scrupulous care was exercised in the preparation of the skin for it has been shown that infection, particularly

TABLE I.—GANGRENE AND LEG SURVIVAL IN TRANSECTION REIMPLATATION EXPERIMENTS

Procedures on femoral artery		Results in leg		
Experiment	No.	Gangrene No.	Viable No.	Viable per cent
Control ligation and Division	12	12	0	0
End-to-end suture anastomosis	12	2	10	83
Arterial graft anastomosis	12	2	10	83
Nonsuture vein anastomosis	12	3	9	75
Polythene plastic anastomosis	5	5	0	0

from gas-forming organisms, will quickly develop in such a devitalized limb (4). The extent of the division of the limb may be seen in the accompanying photograph (Fig. 2).

Reimplantation was begun after encircling the periosteum of the femur in order to insure that no branches of the anterior femoral and median circumflex femoral arteries had escaped section. Mattress sutures in the sheath and substance of the muscle stumps were used for approximation of the muscular mass. During the operation which required 6 to 8 hours, transfusions of whole fresh blood were given since the blood loss was considerable. In the postoperative period a preparation of penicillin in oil and wax was administered to all of these animals in doses of 150,000 units per day for periods of 7 to 10 days. Shortly after operation extensive edema developed below the transection line. Careful postoperative care was necessary for the avoidance of bacterial contamination.

The treatment of the femoral artery differed in each series of transection reimplantation animals. The effect of ligation of the remaining femoral artery was first studied to establish the incidence of gangrene as a control. Four techniques for reuniting the femoral artery were then investigated. End-to-end suture anastomosis was first used followed by a series of animals in which arterial graft anastomosis, nonsuture vein graft anastomosis, and polythene tube anastomosis were employed. Anticoagulants were purposely omitted in these experiments. Of a total of 65 dogs operated upon 53 survived long enough for useful observations. Deaths from shock during operation and early postoperative deaths accounted for 12 animals in which no evaluation of the status of the extremity could be made, except that in no case was the anastomosis defective. There were no animals with gangrene of the leg in the excluded group.

RESULTS

The criterion of failure in each instance was the development of decisive, massive gangrene in the leg beyond the transection site. Skin temperatures were taken at frequent intervals but in these experiments failure of an anastomosis was obvious on gross observation. In Table I the incidence of gangrene in each group of experiments is recorded.

Controls. Division of the femoral artery was performed in a series of 12 dogs subjected to the transection and reimplantation procedure. In this group of animals the only source of blood supply to the extremity beyond the transection was via the femoral artery except for the very small supply within the femur itself. Ligation of the femoral artery was performed at intervals of from 1 to 12 days after the transection reimplantation procedure. Gangrene developed in each of the 12 animals, with the line of demarcation usually falling at the transection incision. Reichert had shown previously in a series of 16 dogs that a limb transected in this manner was dependent upon its arterial supply from the intact femoral artery for a period of at least 14 days. In some animals after 12 or 14 days new vascular channels are formed which seem to be sufficient to maintain viability of the leg. The results in our control group of 12 dogs were in accordance with his findings. The "critical period" during which an anastomosis must function in order to save the leg beyond the transection is, therefore, 12 days in these experiments.

End-to-end anastomosis of femoral artery after transection with reimplantation. Twelve dogs survived transection and reimplantation of the limb with immediate end-to-end suture anastomosis of the severed femoral artery. A simple continuous lock stitch of No. 000000 oiled braided silk upon an atraumatic needle was used for the anastomosis. There were 2 failures. In 1 animal which died on the sixth postoperative day from a perforated duode-

nal ulcer a fine, thread-like thrombus was found at the suture line floating within the lumen of the vessel for a distance of 3 centimeters. This dog's leg might have survived but is included among the failures because of the postmortem findings. The second dog was sacrificed on the seventh postoperative day; extensive gangrene had developed. Gangrene resulted not from thrombosis at the suture line but from injury to the artery near the site at which the arterial clamps had been applied during operation. The 10 remaining dogs maintained viable legs throughout the period of observation. Animals were sacrificed for study at regular intervals from 21 days to 6 months. Pulsations of the femoral artery distal to the anastomosis were present at the time of sacrifice in each animal. In all instances in which the animals were sacrificed the suture line was intact with a smooth intimal surface. Arteriograms, injections of Hill's media, and anatomic dissections were done to check the status of these anastomoses.

Arterial homografts after transection and reimplantation. In 12 animals subjected to the transection-reimplantation procedure a fresh segment of femoral artery from another dog was inserted after division of the femoral artery. The grafted segments measured from 4 to 7 centimeters in length. In addition to restoring circulation this arterial graft procedure effected a bridge and avoided tension. In extensively damaged arteries a "bridging" anastomosis is usually essential in order to avoid tension. The work of Gross and his associates on aortic transplantation suggested to us the use of this method. Previous work by Carrel (5), Watts, and Williamson and Mann has shown that arterial grafts are effective as a means of bridging arterial defects although the experiments of these workers did not include the conditions of maintaining circulation to the leg by means of a single grafted artery. Objections to arterial homografts can be made since late degenerative changes in these grafts have been observed, but such defections occur much later than would influence survival of an extremity in which they might be used. Two dogs were classed as having failures of the arterial graft anastomosis. The first of these developed a perforation measuring 2 millimeters at one of the arterial suture lines on the thirteenth postoperative day, and a large hematoma within the wound was found. No evidence of gross infection was present. The same findings were observed in the second dog which developed gangrene. This animal had a spastic hyperextended limb following the operation. The transected tissues were placed under considerable tension in this position, and at necropsy it was found that the suture had torn through the muscle stumps creating a large dead space across which the femoral artery was strung with little surrounding soft tissue support. Considerable stress and eventual parting of the graft anastomosis creating a perforation through which the hematoma had formed presumably caused this failure on the eleventh postoperative day. It is significant that neither of these animals displayed necrosis of the distal muscles which fact indicates that until the time immediately prior to the accident of perforation the anastomosis had functioned satisfactorily. The 10 remaining animals maintained a warm leg which gradually increased both in function and usefulness.

Fig. 2. Photograph at operation of a completed leg transection designed to interrupt arterial blood supply to the extremity except via the femoral artery.

Fig. 3. Dissection of femoral artery containing a patent and functioning arterial homograft in the case of a dog sacrificed for 5 months after transection and reimplantation. A slight dilatation of the graft may be observed. The musculature below the transection site appears normal.

Four animals were sacrificed from 5 to 10 weeks from the date of operation at which time pulsations below the anastomosis were present. Arteriograms were made, and in each instance the graft was patent with no evidence of constriction. Grossly the anastomoses were well healed. Histologic examination revealed necrosis of one or more layers of the graft wall which in only 1 instance was sufficiently extensive to demonstrate an area of potential weakening of the arterial channel. Fibrous thickening of the intima had occurred in 1 instance, and in another single instance the intima was covered with a very small microscopic thrombus at the site of union of graft to artery.

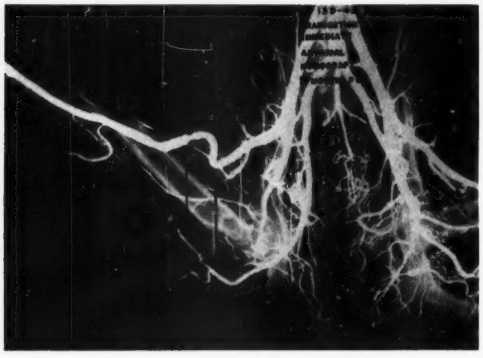

Fig. 4. Roentgenogram of the right leg in an animal sacrificed for study 5 months after transection and reimplantation with an arterial graft (same animal as Fig. 3). The lumen is patent and arteriograms in the living animal using diodrast presented a similar picture.

One animal in which a femoral artery homograft was used in the right leg has been sacrificed at the end of 5 months. The injected arterial tree may be seen in Figure 3 and a roentgenogram of the same appears in Figure 4. A completely open channel may be seen at this time 5 months after insertion of the graft. Arteriograms of this animal during life exhibited the same findings. A photograph of the specimen of this graft may be seen in Figure 5. At dissection slight aneurysmal dilatation of the graft was noted and in a small area there was a lack of intima. There was no thrombus. Five arterial graft preparations have been saved for later study.

Nonsuture vein graft of the femoral artery. In the case of 12 dogs subjected to the transection-reimplantation procedure vein grafts were inserted between the ends of the divided and resected femoral artery. The graft was composed of a segment of the femoral or saphenous vein of the opposite leg secured upon vitallium cuffs in the manner described by Blakemore and his associates. When the saphenous vein was used 2 millimeter vitallium cuffs were employed. It was found that a 3 millimeter cuff and a femoral vein made the best bridge.

Three dogs in the Blakemore-Lord nonsuture anastomosis group developed gangrene of the reimplanted limb and were sacrificed on the fifth, seventh, and ninth postoperative days, respectively. The first failure demonstrated a 5 millimeter thrombus within the dilated vein graft. The clot was adherent to the vein wall at its point of contact at the distal cuff. The second failure showed a 3 millimeter perforation in the wall of the distal arterial stump immediately adjacent to the circumferential ligature. The arterial wall at this point was necrotic. There was a large hematoma in the thigh. The vein graft of the third failure was found on postmortem examination to have been completely extruded from the ends of the divided femoral artery. The vein was attached securely to the vitallium cuff at each end and was dilated in an aneurysmal fashion and filled with an organizing clot which completely obstructed the lumen. Nine dogs maintained warm, viable limbs which gradually recovered normal ap-

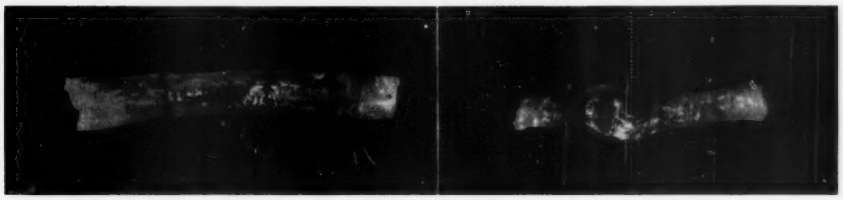

Fig. 5. a, left. Femoral artery homograft removed on thirty-seventh postoperative day. b, Femoral artery and homograft removed 5 months after insertion (same as Figs. 3 and 4). Dilatation of the graft and slight loss of intima may be seen.

pearance and function. As the postoperative edema subsided femoral arterial pulsations became palpable proximal and distal to the transection line. All but 1 animal, however, suffered gradual diminution and ultimate obliteration of these pulsations within ensuing weeks. Seven animals demonstrated an anatomic failure of this technique of bridging arterial defects within varying periods of from 16 to 37 days after the completion of the anastomosis, although from a functional standpoint this anastomosis served beyond the time necessary for collaterals to develop and take over the burden of blood supply to the leg. An eighth animal sacrificed on the ninetieth day after vein anastomosis was found to have an occlusion. In the case of the ninth animal, on clinical examination the vein graft was still functional after 15 weeks. In each of the instances mentioned failure was confirmed by dissection of the graft from the transected limb at which time it was common to find dissolution of the venous segment, extrusion of one or both cuffs from the ends of the femoral artery, or more rarely aneurysmal dilatation of the vein graft with organized clot within its lumen. Circulation had been maintained by the establishment of collateral vessels across the transection scar.

Plastic tube prosthesis after transection and reimplantation. The polythene tube prosthesis experiments were purposely made as simple as possible in an effort to determine if a simple and crude device could serve as an adequate means of replacing a destroyed segment of an arterial trunk during a critical period (estimated at 14 days). So-called "medical" or nonreactive polyethylene tubing was cut in sizes measuring 2 to 4 centimeters, the lumen corresponding approximately to that of the femoral artery. The rough ends were polished in order to eliminate unnecessary trauma to the arterial intima but they were not tapered externally nor flared on their inner surfaces. Five dogs were subjected to transection and reimplantation of the limb and insertion of such a prosthesis within the divided ends of the femoral artery. The tube was maintained in place by means of a single circumferential ligature around the overlying arterial wall at each end. Each dog developed gangrene of the distal limb; 3 by the fourth day, 1 by the sixth, and 1 by the tenth postoperative day. In each instance the tube was tightly plugged with an organizing thrombus limited to the lumen of the tube. None of the circumferential ligatures appeared to have damaged the arterial wall in this short time. Each animal developed a cold, discolored, pulseless leg. This method of arterial anastomoses was not investigated further. Plastic materials have been fairly well proved to be unsuccessful in blood vessel anastomosis work except in the aorta (12), although heparinization of animals may prolong the period during which they remain patent (21).

DISCUSSION

It would seem the anastomosis of arteries presents no great obstacle to success in salvaging the leg with arterial injury. The poor clinical results obtained in World War II must have been related to the deleterious effects of long periods of ischemia in the first place and perhaps infection secondly. Early restorative surgery with arterial anastomosis should greatly reduce the incidence of gangrene accompanying injuries. Direct end-to-end suture of severed arteries is the operation of election for arterial severance but the major-

ity of arteries injured have sustained or required some sacrifice of their substance. To avoid the danger of separation of the anastomosis a bridging anastomosis is required. The experiments herein reported indicate that an arterial graft taken from another subject might be the method of choice in such cases since in these experiments it has proved somewhat superior to other procedures. Gross has demonstrated the usefulness of large preserved grafts in his work on transplantation of the human aorta. In experiments to be reported later, preserved arterial grafts have been proved equally as efficient as fresh ones in femoral artery anastomosis. These statements are true for immediate survival of critically ischemic extremities and for the early postoperative results in animals in which these techniques have been used. The nonsuture vein graft is a valuable technique and proved efficient during the critical period up to the time when collateral circulation is developed in the transected leg. It does not remain patent, however, as long as the arterial graft. It effects a less secure junction of the vessels and technical difficulties are more frequently encountered when such a procedure is carried out.

Plastic tubing or other inert materials should not be used for the anastomosis of small arteries since other methods are greatly superior. While it may be possible to prolong the time before clotting occurs in these tubes by using anticoagulants the control of clotting in patients is not accurate enough under usual circumstances and is too hazardous in the wounded.

In military surgery some plan for the early detection and rapid evacuation of patients with arterial injuries is needed. In addition, early anastomosis of severed arteries must be practiced in every possible case. Teams experienced in the operative techniques of arterial anastomosis would be a desirable complement to this project.

SUMMARY

In the experiments presented herein it has been shown that arterial reunion by end-to-end suture, arterial homograft bridge, and nonsuture vein graft was highly successful in clean wounds when it is performed immediately after arterial severance. All methods of anastomosis were tested in a highly critical preparation, the transection-reimplantation procedure of Reichert in which it has been shown that the viability of the leg beyond the transection depends upon the single artery under investigation, in this case the femoral artery. Adjunctive collateral routes in the soft tissues are entirely interrupted and ligation of the femoral artery in a group of control animals subjected to transection resulted in massive decisive gangrene in all cases when the procedure was done within 12 days of operation.

The techniques for arterial anastomosis which include an intima-to-intima approximation were successful in sustaining a current of blood in the femoral artery during a critical period when collateral routes were interrupted in 75 per cent of animals when the nonsuture vein graft was used and in 83 per cent of animals when end-to-end arterial suture anastomosis or arterial graft anastomosis was employed. Failures were the result of technical errors and accidents rather than spontaneous intravascular clotting at the anastomosis site. Immobilization and other control measures which are possible in human subjects are not feasible in dogs. These results were secured without using heparin or other anticoagulants in work on relatively small arteries in which heparinization might be thought necessary. The known difficulties and dangers which accompany the use of these drugs in open wounds and in patients with multiple injuries make this finding clinically important.

The simple method of joining arteries by using unlined plastic tubing was employed to some extent in World War II and is an attractive one because of its simplicity. No legs survived in the experimental animals of this study in which polythene tubes were used for anastomosis. Rapid formation of an obstructing thrombus regularly occurred very early in the postoperative period.

Almost normal leg function was the usual late finding in dogs which had successful immediate reimplantations with arterial anastomoses.

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ON THE OCCURRENCE OF EPITHELIUM AND GLANDS OF THE INTESTINAL TYPE IN THE GASTRIC MUCOSA

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THE specialized literature of pathology makes it clear that cells ordinarily distinctive of the intestinal epithelium may at times be found in the stomach. Even though this remarkable heterotopy is a relatively common occurrence, its existence and significance have been disregarded, strangely enough, by textbook writers in this country. As a result, students, clinicians, and some pathologists, at least, are unaware of the facts and implications connected with this phenomenon.

The characteristic intestinal elements occurring under certain conditions in the stomach lining are of three kinds: (1) columnar cells, with a cuticular border on their free surface; (2) goblet cells, distended with mucus; and (3) Paneth cells, containing brightly staining, acidophilic granules. The first two cell types are found in the layer of epithelium that serves as a surface covering of the gastric mucosa and lines the foveolae that dip below the general surface level. All three types occur as components of epithelial tubes that extend downward from the foveolae and come to resemble the intestinal glands (of Lieberkuehn). As a fourth type might be listed the argentaffin cells which are wedge-shaped elements that blacken with silver treatment and thus become revealed along the basal surface of the epithelium; these elements are most numerous in the intestine (and particularly in the intestinal glands) but do occur sparsely in the normal stomach as well. When islets of the intestinal type occur in the stomach, their number increases greatly.

Kupffer (1883) was the first to record the presence of intestinal elements (goblet cells; columnar cells with borders) in the gastric epithelium. Contrary to Kupffer and numerous others who regarded these structures as normal occurrences, Schmidt (1896) made the important observation that it is in conditions of chronic inflammation that the gastric epithelium may transform into a type resembling the epithelium of the intestine. This conclusion has been upheld by the studies of Chuma (1923), Moszkowicz (1923), Konjetzny (1928), Magnus (1937), and others. Chronic inflammatory conditions, such as accompany ulcer and carcinoma of the stomach, exert a destructive effect upon the gastric mucosa, and especially upon its specialized gastric glands, whereupon the more resistant foveolae regenerate tubules that take on the appearance of intestinal glands.

The significant literature on this subject is almost exclusively German. The failure of American investigators to participate significantly in this particular field is exemplified by Meissner (1947) who reported on the distribution of parietal cells in 80 cases of gastric carcinoma and 39 cases of gastric ulcer, yet did not record any metaplasia of this type. It is, nevertheless, difficult to explain the almost unanimous omission of such a conspicuous metaplasia from general textbooks of pathology published in this country. Of nine current texts designed for teaching and reference, only one (Boyd, 1943) gives the matter correct citation, and here it is not considered under chronic atrophic gastritis, as such, but rather in the relation of carcinoma to this condition. Karsner (1942) is the only other text to refer to this topic, and then, unfortunately, under hypertrophic rather than atrophic gastritis; even more regrettable is his resurrection of the early and thoroughly discredited concept of "*aberrant* islands of intestinal glands, frequent in the (normal) stomach." Bell (1947) presents a photomicrograph that shows numerous goblet cells in a section illustrating the altered mucosa in chronic atrophic gastritis, but fails to comment on this either in the figure legend or in the text.

From the Department of Anatomy, Northwestern University Medical School.

Contribution No. 518 from the Anatomical Laboratories of Northwestern University Medical School.

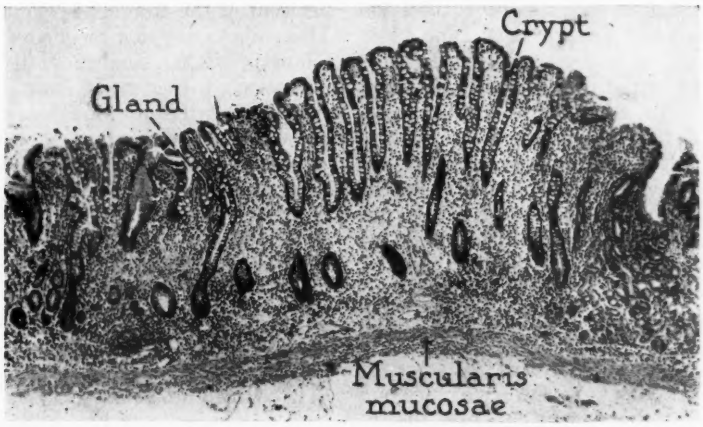

Fig. 1. Vertical section of the gastric mucosa from a portion of a stomach resected for carcinoma. Photomicrograph; ×41. The area shown belongs to the lower corpus but is at some distance from the carcinomatous site. It illustrates the changes attendant on chronic atrophic gastritis. Glands are regenerating from the resistant crypts; the great number of goblet cells in its altered epithelium is obvious, but other changes are not seen to good advantage at this low magnification.

Ewing (1940) in his monographic work on neoplastic disease briefly but correctly cites the tendency toward "a metaplastic transformation of gastric into an intestinal type of cell lining" as a concomitant of stomach cancer. Among the more pretentious reference works in clinical medicine, Bockus (1943) typifies the silence on these matters which was broken by Schindler's contribution to Portis's (1944) *Diseases of the Digestive System* and by his own work, *Gastritis* (1947). The reason why the last named author is unusually aware of the relation between gastritis and this type of metaplasia is explained by his European background in research on gastric pathology.

DESCRIPTION OF SPECIMEN

The present writers became interested in this particular phase of pathology when one of us (R. T. B.), on examining a histologic section taken at some distance from the site of a gastric carcinoma, for which he had done a

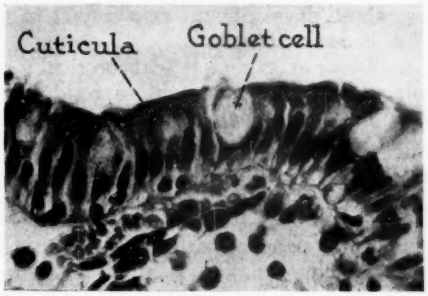

Fig. 2. Detail of the mucosa as in Figure 1. Photomicrograph; ×515. The region shown belongs to the lining of a crypt, at its mouth. The simple columnar epithelium shows both goblet cells and a discontinuous cuticular border; both of these features occur in the normal intestine, but not in the stomach.

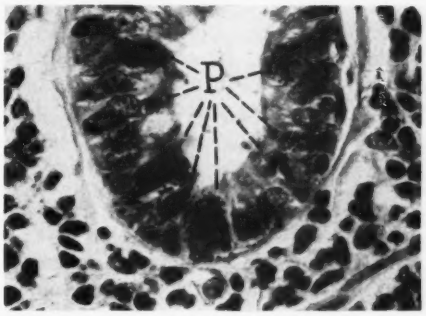

Fig. 3. Detail of the mucosa as in Figure 1. Photomicrograph; ×275. The region shown is the basal end of a regenerating gland. In it, Paneth cells (*P*) with bright acidophilic granules occur abundantly; this cell is a characteristic feature of the intestine, but not of the normal stomach.

resection, questioned the proper identification of what looked like Paneth cells. The slides and a piece of the excised gastric wall were brought to the senior author (L. B. A.) who has studied them, made additional sections, and prepared the present report. The appearance of typical regions of the mucosa, affected by the attendant chronic atrophic gastritis, is shown in Figures 1 to 3. They conform to the heteroplastic alterations seen by previous investigators, and their main features are so easily discernible that the figure legends will suffice as descriptions.

DISCUSSION

The essential facts as to the occurrence of a metaplasia of gastric epithelium into the intestinal type of epithelium have been established firmly, and the present writers can scarcely hope to do more than give some neglected publicity to such a fundamental alteration and to present some of the conclusions, evaluations, and interpretations that relate to it. This discussion is based mostly on an analysis of a fairly extensive literature and a synthesis of the facts and evaluations thus gained. Numerous questions naturally arise concerning these areas of heteropic, intestinal type of mucosa; on the whole, the answers rest on a fairly firm basis of fact and logical inference, but some (paragraphs 7 and 8) are frankly speculative, although consistent with information supplied by experimental embryology.

1. *Size, shape, and distribution.* The size of altered areas ranges from tiny islets less than a millimeter in diameter, through large patches, to total (or nearly total?) replacement of the entire gastric mucosa. The affected areas may occur as rounded islets or extend irregularly into elongate rays; presumably serial reconstructions would demonstrate much more of a connecting pattern than random sections show, but this has never been done. The pyloric antrum is the commonest site of this heteroplastic change, but it may extend into the body of the stomach and beyond or occur diffusely throughout the stomach lining.

2. *Frequency.* Various surveys record the occurrence of intestinal mucosa in 11 to 100 per cent of the stomach specimens examined. This wide variation is reconciled in part by the following facts, singly or in combination: (1) selected specimens from patients with chronic gastritis give much higher frequency values than does random sampling from unselected autopsies; (2) increased frequency of occurrence goes parallel with the severity of the chronic inflammatory disturbance, and thus tends to run higher in series involving carcinoma than in ulcer series; and (3) the frequency reported by any worker bears a direct relation to the size and number of areas of the stomach that were studied microscopically in his series.

3. *Normal or pathological nature.* Famous names (Kupffer; von Ebner; Stoehr; Schaffer) of an earlier day were among those who considered the intestinal type of epithelium to be an occasional constituent of the normal stomach. Against the view that the islets represent congenital anomalies of any sort is the fact that they do not occur in late fetuses or infants. Opposed to the view that they are normal, postnatal developments is the fact that islets of an intestinal character have never been demonstrated in an indisputably normal stomach at any age. On the contrary, there is a high correlation between the occurrence of an intestinal type of epithelium in the stomach and the presence of long standing inflammation there. Their appearance is a part of the characteristic picture of chronic atrophic gastritis, especially such as results from an ulcer or carcinoma. It is a pathological phenomenon whose development, as a sequel to gastritis, is demonstrable.

4. *Source of origin.* It is theoretically possible to attribute an origin to residual embryonic cells that had been a part of the epithelial lining of the stomach since the embryonic period; at some later date these would first arouse from slumber and express themselves differently from their neighbors (although still operating within the limits of their latent pluripotentialities). Such an interpretation, however, is incapable either of substantiation or direct refutation. In the same category of hypothesis is the alleged physical displacement, during the early development of the gut, of cells of the embryonal intestine

that later become activated and express their hitherto slumbering, normal potentialities. More tangible is an explanation based on an actual invasion of the stomach by fully differentiated intestinal mucosa, but specimens showing a diffuse dispersion of islets throughout the entire stomach and the lack of sufficient evidence in the pyloric canal, where an invasion should be most prominent, engender no enthusiasm for this theory. Eliminating all but the ordinary stomach cells as the source of origin, it has been suggested that the intestinal elements arise directly by a kind of regression or a mucous degeneration; no evidence favors such an interpretation. Actual observation indicates that the intestinal type of epithelium does, indeed, develop *in situ* in regions where the epithelium, and especially that of the glands, has been destroyed by the inflammatory process. But it is proliferation from the depths of the resistant foveolae that furnishes elements which move out into the surface layer; in the opposite direction, down-growing buds appear and produce tubes that take on the characteristics of intestinal glands.

5. *Metaplastic nature of origin.* There is no evidence in the stomach or elsewhere in the body of a direct transmutation of one type of fully differentiated cell into another mature type. Rather, the foveolar cells first dedifferentiate and return to a more generalized type; both the cytoplasm and the centrally located nucleus stain darkly with basic dyes. Then the cells proliferate and enter into specializations, but this time some unconformists take new directions and arrive at other endpoints than did their precursors in normal fetal histogenesis. The full course of happenings is one of true metaplasia.

6. *Identity with intestinal mucosa.* As far as can be seen, the columnar cells with striate borders, the goblet cells and the Paneth cells are all identical with their counterparts in the intestine. The general morphology of the tubular glands and certain details of their arrangements, such as the basal position of Paneth cells and the distribution and increased abundance of argentaffine cells, further strengthen the conclusion that this is a case of essential identity and not of mere counterfeit similarity.

7. *Cause of metaplasia.* The idea that the intestinal type of epithelium is of a "lower" order than gastric epithelium and that the regenerating tissue is somehow stopped along its course at the intestinal stage of differentiation, involves a gratuitous assumption of what is "high" and what is "low," as well as the erroneous belief that this particular sequence of stages takes place in the normal developmental or regenerative course in the stomach. Basic to any consideration is the more fundamental question as to why the embryonic gut, during its histogenesis, indulges in quite different types of specialization at different levels. Following directly on the heels of this query is the closely connected one as to why the regenerating epithelium of the chronically inflamed stomach may, on occasion, act as does the epithelium of the normally differentiating intestine in the embryo. Since it has been shown in this laboratory that a normal stomach can regenerate its characteristic epithelium and organize its typical gastric glands when areas of mucosa are removed experimentally (Ferguson, 1928), one is led to the conclusion that there must be something about the inflamed stomach that conditions the differentiation of an intestinal type of epithelium and gland. What this factor may be is suggested by the modern lore of causal embryology (*cf.* Needham, 1942). In normal or experimentally altered development, various embryonic organs and parts are "induced" to develop in a certain way at a definite moment because of chemical substances emanating from contiguous parts. The relation of an epithelium to its substrate is intimate. It is possible that the altered chemical nature of the inflamed tunica propria of the gastric mucosa is the factor influencing the abnormal result achieved during epithelial regeneration and histogenesis in this instance. Such a result finds its parallel in the induction of the optic vesicle by the adjacent mesenchyme in the head of an embryo.

8. *Ultimate fate of islets.* It is known that the intestinal type of organization can still be found in islets of the gastric mucosa even when scars are the only easy clue to the occurrence of an earlier ulcer and its attendant gastritis. Yet it is held probable that islets can revert

eventually to the ordinary type of gastric cells and glandular morphology. This they would do, not by a direct transformation and remolding of cells already specialized into intestinal types but by cellular replacement and rebuilding. Following the line of reasoning advanced in the previous paragraph, one might suggest that when sufficiently normal conditions are restored in the mucosa, the replacing cells arising from foveolae then find themselves in a chemical environment characteristic of that normal region and accordingly express themselves in the manner of differentiation customary to that region.

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CLOSURE OF THE PATENT DUCTUS BY SUTURE-LIGATION TECHNIQUE

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SINCE 1938 when Dr. Robert E. Gross (6) performed the first successful closure of a patent ductus arteriosus, considerable interest in this procedure has been taken by thoracic and general surgeons alike. There is good agreement on the beneficial results of closure of the ductus, but some difference of opinion exists as to the best method of closure. Gross (5) used simple ligation of the ductus in his first 14 patients, but then abandoned this method because of evidence that complete closure was not obtained in several instances. He secured somewhat better results in his next 29 patients by the use of a method employing cellophane in conjunction with ligatures. Some untoward experiences with this method, however, resulted in the development of a technique for complete division of the artery. In 1944 Gross (5) reported 14 successful divisions of the patent ductus and since that time has used complete division in a large number of cases. It is his belief that division is the procedure of choice in the majority of cases of patent ductus arteriosus.

In 1946 Dr. Alfred Blalock described a method of closure of the ductus based on the use of multiple suture ligatures without division of the artery. At that time he had employed the method successfully in 7 patients with no evidence of recurrence following operation. Blalock expressed the opinion that division and closure of the ductus was an unnecessarily hazardous undertaking, and that by the suture-ligation technique, closure of the ductus could be satisfactorily accomplished without subjecting the patient to so much danger from uncontrollable hemorrhage. It is the purpose of this report to demonstrate the success of the suture ligation method of closure of the ductus as used in the Johns Hopkins Hospital.

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CASE MATERIAL

One hundred and eighty patients with patent ductus arteriosus have been subjected to operation at the Johns Hopkins Hospital during the period October 1, 1942 to December 31, 1948. The majority of the patients were studied preoperatively and referred by Dr. Helen B. Taussig and her associates in the Cardiac Clinic of the Harriet Lane Home of the Johns Hopkins Hospital. A detailed study of the cardiologic aspects and the diagnostic criteria employed in this group of patients is being reported by Wells and Lynxwiler. Most of these patients were children in the age group of 4 to 12 years, the youngest patient being 8 months of age, and the oldest 39 years. Approximately one-fourth were adolescents and young adults. The predominance of females over males in this series is in accord with previous reports, there being 123 females (68 per cent) and 57 males. Nine negro patients with patent ductus were operated on in this group.

By far the greatest number of patients had no significant limitation of activities referable to their cardiac status before operation. Thirty-two individuals, however, had a severe degree of limitation. Many of these represented the more complicated forms of cardiac defects in which the patent ductus was associated with a defect of the interauricular septum, interventricular septal defect, rheumatic heart disease, or superimposed subacute bacterial endocarditis. Five patients were subjected to operation for closure of the patent ductus during episodes of active subacute bacterial endocarditis. Seven others gave a history of previous infection with Streptococcus viridans which had successfully cleared before admission to this hospital.

OPERATIVE TECHNIQUE

In the earlier part of this series simple ligation of the ductus was utilized, but since the

OPERATIVE EXPERIENCE WITH PATENT DUCTUS ARTERIOSUS

October 1, 1942 to December 31, 1948

Procedure	Number of patients	Deaths	Recanalization
Ligation only	9	0	1
Division	7	1	0
Attempted closure	3	2	–
Suture ligation	161	2	0
Total	180	5	1

development of the suture ligation method this procedure has become the standard method of closure of the ductus in this clinic. The operative technique employed in this method has been described by Blalock. Briefly, it consists of the use of the left anterior intercostal approach and exposure of the mediastinum as described by Gross (4). The mediastinal pleura is incised between the phrenic and vagus nerves over the region of the ductus. The pleural flaps are reflected, exposing the pulmonary artery, the aorta, the ductus, the left vagus, and the left recurrent laryngeal nerve. The recurrent laryngeal nerve is followed down under the ductus and the ductus then dissected free of its investing areolar tissue. The dense fibrous tissue between the posterior aspect of the ductus and the left bronchus is divided. The pericardial reflection frequently encountered on the pulmonary end of the ductus is dissected upward, exposing the entire length of the ductus arteriosus and adjacent aorta and pulmonary artery. Temporary occlusion of the ductus for 3 to 5 minutes with a bulldog clamp is advisable in order to observe the immediate effects of closure on cardiac action. Pursestring sutures of medium silk on French or atraumatic needles are placed at the two ends of the ductus, catching the adventitia in several places. These sutures are not tied tightly but with enough tension to stop the flow of blood through the ductus. Two through-and-through mattress sutures of silk are placed through the ductus between the 2 pursestrings and tied tightly so as to encircle the artery completely. All sutures are spaced as far apart as possible. Lastly, a ligature of heavy (No. 4) braided silk or of umbilical tape is tied down over the 2 mattress sutures. While French needles are adequate for placing these mattress sutures, the use of No. 00 or No. 000 silk on atraumatic needles facilitates this step considerably. The mediastinal pleura is closed, the lung re-expanded, and closure of the chest wall carried out in layers.

By this simple technique the operation can usually be completed within an hour or less. The anesthesia of choice is intratracheal cyclopropane and ether with closed to and fro carbon dioxide absorption technique. Before beginning this procedure a cannula is always inserted into an ankle vein for constant venoclysis. Blood is always held in readiness but has been used infrequently.

OPERATIVE EXPERIENCE AND MORTALITY

In the accompanying table is presented a summary of the operative experience with closure of the patent ductus in 180 consecutive cases in this hospital. These 180 operations for patent ductus have been performed by 14 different members of the surgical staff. About one-third of the cases have been operated on by members of the resident staff. The sole recurrence in the entire group was in a patient with active Streptococcus viridans infection whose ductus was closed with 2 braided silk ligatures in the early part of the series. A successful secondary closure was carried out 3 weeks later, but the bacterial endocarditis persisted, and the patient died 3½ months after the second operation.

In the early part of the series 9 patients were treated by simple ligation of the ductus with one or two encircling ligatures of heavy silk or umbilical tape. There were no operative deaths in this group of patients, but one recurrence necessitated a secondary closure. This method has now been entirely abandoned.

In 7 instances, division and closure of the ductus was carried out. In some of these cases the method of division and suture described by Gross (5) was used; in the others the ductus was divided between suture ligatures after pursestring sutures of silk had been placed at the ends of the ductus. In the majority of these cases the ductus was unusually long. One death occurred from postoperative hemorrhage subsequent to division of the ductus between suture ligatures. This death should

have been prevented. At operation it was noted that the ductus was a long narrow vessel and that occlusion of the ductus did not abolish the thrill in the pulmonary artery. The operator was in doubt as to the patency of the ductus and proceeded to divide the vessel between suture ligatures to clarify this point. At autopsy the aortic stump of the ductus was found to be open, the suture ligature having slipped off.

In 3 patients with patent ductus arteriosus attempts at operative closure were unsuccessful. One of these patients had severe dorsal scoliosis and kyphosis. At thoracotomy, which was carried out through the left anterior intercostal approach, the ductus was found to lie well over to the right of the spine and could not be satisfactorily exposed for closure. A secondary attempt at closure of this ductus is contemplated. In the second patient in this group fatal ventricular fibrillation developed during operation just after the chest had been opened. Cyclopropane anesthesia was being used. The child died before the ductus could be exposed. Autopsy showed not only a patent ductus but a coarctation of the so called infantile type proximal to the ductus. The third patient represents the only fatal operative accident of a technical nature in this series. In this patient, a child of 6 years of age with an uncomplicated patent ductus, injury to the pulmonary artery during dissection of the ductus resulted in death on the operating table from uncontrollable hemorrhage. At autopsy a laceration of the pulmonary artery at the base of the ductus was seen. This case emphasized a technical point in mobilization of the ductus which has been made by Touroff; namely, in dissection around the ductus the operator should follow the plane near the aortic end of the vessel so as to avoid damage to the thin-walled pulmonary artery.

Closure of the ductus by the multiple suture-ligation technique has been used in 161 cases. No case has been encountered since the adoption of this procedure in which this method has proved to be inapplicable. There was one operative accident related to the employment of this suture-ligation method of closure of the ductus which should be described in detail. In 1 patient, a child of 4 years, a large ductus had been dissected free and pursestring sutures had been placed at either end. When the operator tied the pursestring suture at the aortic end of the ductus he tied it extremely tightly and tore the ductus completely out of the wall of the aorta. The ensuing hemorrhage was controlled by clamping the aorta proximal and distal to the ductus and suturing the defect in the aortic wall. Fortunately the child survived but only after vigorous resuscitative measures had been instituted. This accident illustrates the danger of too much tension on the pursestring suture at the end of the ductus. It should be emphasized that the pursestring sutures at the ends of the ductus are tied snugly but not tightly.

There have been 2 postoperative deaths in this group of 161 patients with patent ductus closed by the suture-ligation technique. Both patients were children aged 2 and 3 years, respectively, and in each instance death occurred in the first 24 hours following uneventful closure of a seemingly uncomplicated patent ductus. In both children generalized convulsions and hyperpyrexia developed shortly after their return from the operating room. These symptoms were associated with extreme tachycardia and profound vasomotor collapse. Despite vigorous therapeutic efforts, persistence of these symptoms resulted in death within 12 and 24 hours respectively. Autopsy was not permitted in the 1 case, and in the other, postmortem examination failed to show any satisfactory explanation for the terminal symptoms. Closure of the ductus had been satisfactorily accomplished.

The over-all operative mortality in this group of 180 cases of patent ductus arteriosus was 2.7 per cent. In the 161 cases of patent ductus closed by the suture-ligation technique the operative mortality was 1.2 per cent.

POSTOPERATIVE MANAGEMENT AND COMPLICATIONS

In a great majority of these patients the postoperative course was remarkably smooth and without significant complications. Their care after operation has become fairly well standardized. On return from the operating room they are usually given oxygen for 6 to 12 hours, and supplemental parenteral fluids

are used for the first 12 hours. Penicillin is administered in full doses for the first 5 to 7 days. Unless coexistent cardiac defects prevent, the patients are permitted to sit up on the second or third postoperative day, and are usually ambulatory by the fifth day. The majority of patients have been allowed to leave the hospital by the eighth to tenth day after operation.

There have been no instances of wound infection or empyema following operation in this group of 180 patients with patent ductus arteriosus. Two of the 5 patients, who had active bacterial endocarditis, had persistently positive blood cultures following operation. One of these patients also had an interauricular septal defect. Despite successful closure of the ductus in these 2 patients, persistence of the bacterial endocarditis resulted in death 2 and 3 months, respectively, after leaving the hospital.

Hemothorax of significant degree has been encountered in only 1 patient, and was cleared satisfactorily by multiple thoracenteses. In 7 other patients a single postoperative thoracentesis was carried out to remove small serosanguineous collections in the left pleural cavity. There were 2 instances of postoperative atelectasis and 3 cases of bronchopneumonia. Paralysis of the left vocal cord developed in 2 patients following operation, although great care is always taken during operation to avoid damage to the left recurrent laryngeal nerve. In both of these instances, fortunately, this paralysis was transitory. Eleven patients have had evidence of congestive heart failure after operation which necessitated digitalization. All but 2 of these had an associated septal defect. One child, 4 years of age, had an unexplained cerebrovascular accident characterized by coma, convulsions, and hemiplegia which persisted for several days and then cleared spontaneously without any residuum.

FOLLOW-UP STUDIES

A majority of these patients have been followed after discharge from the hospital by Dr. Helen Taussig and her associates in the Cardiac Clinic of the Harriet Lane Home. In uncomplicated cases the patients have been seen routinely 1 week after discharge and thereafter at intervals of 6 and 12 months.

Recanalization of the ductus following operative closure in these 180 patients has been encountered in only one instance, the patient described above with active bacterial endocarditis whose ductus had been closed by simple ligation. Successful secondary closure was subsequently performed in this patient. In none of the other patients has there been any evidence of reopening of the ductus.

In all of the 161 cases of patent ductus closed by the suture-ligation technique there has been disappearance of the continuous murmur with no suggestion of recanalization to date. Of these patients, 126 have now had adequate follow-up studies over a period of time ranging from 6 months to 6 years. The remainder have been operated on since July 1, 1948. In only 1 case has there been an opportunity to examine anatomically a ductus closed by the suture-ligation method at a significant period of time after operation. This patient, a woman of 24, died of a spontaneous subarachnoid hemorrhage 1 year after successful closure of her patent ductus by the suture-ligation technique. At autopsy the ductus, which measured 1 centimeter in length, was found to be completely obliterated by a solid core of fibrous tissue. Serial sections taken through the ductus showed complete obliteration of the lumen of the vessel by fibrous tissue with no tendency to recanalization. There was no evidence of persistence of any endothelial elements in the obliterated ductus. An endothelial cushion had completely sealed off the ductal opening in the lumen of the pulmonary artery and of the aorta.

A detailed evaluation of the degree of improvement obtained by closure of the ductus in this group of patients is being reported by Wells and Lynxwiler. By far the greater number have shown significant improvement. In some of the more complicated cases in which a small ductus was associated with a large defect of the interauricular or interventricular septum there has been little or no apparent improvement following closure of the ductus. However, closure of a large ductus has proved to be quite beneficial to many of the patients

with coexisting septal defects. In one 4 year old colored child closure of the patent ductus has resulted in functional improvement and relief of congestive failure, but progressive cyanosis, clubbing, and polycythemia have developed.

COMMENT

In 1947 Shapiro collected and reviewed 626 operative closures of the patent ductus carried out by 46 different surgeons. The incidence of recanalization of the ductus when closed by various forms of ligation (431 patients) was found to be 7.8 per cent. Because of this incidence of recurrence Shapiro concluded that ligation of the ductus should not be done if section is possible.

In the Johns Hopkins Hospital 161 closures of the patent ductus have been done by the suture-ligation method previously described without a single instance of recanalization. This technique of closure of the ductus in continuity has been applicable to all cases encountered since its adoption and has proved to be a satisfactory method of producing and maintaining obliteration of the patent artery.

Gross (3) has reported a series of 180 complete divisions of the ductus with only 4 deaths, none of which was from hemorrhage. In his hands division of the ductus is obviously a safe and definitive method of closure; however, it seems improbable that this low mortality rate in division of the ductus can be maintained by less experienced operators.

In 161 suture-ligation closures of the patent ductus at the Johns Hopkins Hospital there have been 2 deaths. These operations have been done by 14 members of the surgical staff. About one-third of the patients have been operated on by members of the resident staff.

We agree with Gross (3), Wangensteen, Potts, Crafoord, Jones, and others that division and closure of the ductus is a better surgical procedure from a strictly technical viewpoint. On the other hand, if a simpler and less dangerous procedure will produce the same result, there are indications for its use. It should be understood that we are not advocating the use of simple ligation of the ductus but rather the use of the suture-ligation method of closure described herein. Some of the advocates of division of the ductus, such as Wangensteen, have inadvertently left the impression that simple ligation of the ductus is used in this clinic, whereas in reality the use of multiple suture ligatures is a vastly different technique.

This method of closure of the ductus, by its inherent simplicity and safety, may lend itself more appropriately to general application than a technique of complete division.

SUMMARY

One hundred and eighty patients with patent ductus arteriosus have been operated on at the Johns Hopkins Hospital during the period October 1, 1942 to December 31, 1948 with 5 deaths and 1 instance of recanalization. Simple ligation was used in this latter case.

In 161 closures of the patent ductus by suture-ligation technique 2 deaths have occurred but no instance of recanalization.

The suture-ligation method, because of its simplicity and safety, is advocated for general application in preference to a method of division of the ductus.

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INGUINAL HERNIAS, ABSENCE OF THE UTERUS, AND PSEUDOHERMAPHRODITISM

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CONGENITAL abnormalities of the uterus are common, but complete absence of the uterus is extremely rare, for the organ is represented by at least a nubbin or undeveloped tube of uterine tissue in most cases of its apparent absence (Jarcho, 1946). Such a congenital anomaly suggests the presence of another. In the 3 typically feminine patients now described there was absence of the uterus. In the first there was a normal vagina and bilateral inguinal ectopia of the ovaries, undeveloped tubes, and probably also uterine rudiments. In the 2 other patients, who were sisters, there was absence of the upper vaginal segment, and bilateral inguinal ectopia of undeveloped tubes, uterine rudiments, and testes thought at first to be ovaries.

CASE REPORTS

CASE 1 (R. I. No. 94634/48). M. S., a housewife aged 27 years, was admitted to the Radcliffe Infirmary on October 19, 1948, for operative treatment of her bilateral inguinal hernia.

A reducible swelling had been present in her right groin for as long as she could remember. This caused her little inconvenience until the beginning of 1948, when it began to ache on exertion. About the same time she first noticed a swelling in the other groin. The symptoms showed no periodicity. Her breasts and secondary sex characteristics had developed at the usual time, but she had never menstruated, nor had there been any recurring lower abdominal pain. She had led a normal married life since 1946, although a gynecological examination in 1941 had failed to demonstrate a developed uterus. In consequence she had intended to adopt a baby in the near future. There was no relevant previous or family history.

The patient was cheerful, healthy, intelligent, and typically feminine. Her breasts were well developed and the external genitalia were normal, but the pubic and axillary hair was soft and limited in extent. On pelvic examination, although the vagina was of normal size and length, the cervix, uterus, and adnexa could not be felt. Examination of the inguinal canals revealed globular swellings on both sides when the patient strained; these were controlled by pressure over the internal rings. The swelling on the right side was more marked and it was possible to get above its ovoid distal portion, which measured some 4 by 3 centimeters and lay in the long axis of the canal. Neither swelling was tender. There were no other abnormalities on clinical examination, and an intravenous pyelogram showed that there was no associated congenital anomaly of the renal tract.

Under general anesthesia, a single, curved, skin-crease incision was made and the inguinal canals were exposed by a division of the external oblique aponeuroses.

The right inguinal canal contained a short, thick round ligament, attached to a smooth, extraperitoneal structure which was assumed to be a normal right ovary, and to a solid tubular structure, 1 centimeter in diameter, which passed in a vascular pedicle through the internal ring into the pelvis. It was not possible to define a hernial sac on this side.

On the left side, the round ligament was again shorter and thicker than normal, and the sac of an obvious sliding hernia of the ovary was defined and opened anteriorly. This exposed an ovary similar to that on the right except for a clear cyst 1 centimeter in diameter, and again a tubular structure 1 centimeter in diameter, passing with a vascular pedicle into the pelvis.

The tubular structures were now palpated by one finger in the vagina, and one introduced through the left hernial sac, and each band passed medially without expanding, to fuse smoothly with its fellow above the vagina. There was no fimbriated extremity laterally near either ovary, nor was there a peritoneal fold in the midline between the bladder and the rectum. Biopsies were not taken and the peritoneum was closed. Only when the round ligaments had been divided were both ovaries easily reduced through the widened internal rings. The transversalis fascia was approximated to the inguinal ligament by interrupted nylon stitches and the repair completed by one layer of the nylon darn recommended by Moloney and associates (1948). The external oblique was repaired with nylon and the wound was closed. The patient was discharged home on the 10th postoperative day, with the wound well healed.

Biochemical investigation. The androgen excretion was 21 milligrams per 24 hours. (This value is considered to be at the upper limit of normal for women.)

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CASE 2 (R. I. No. 16806/48), and CASE 3 (R. I. No. 17112/48). Two unmarried sisters were admitted to the Radcliffe Infirmary on November 10, 1948, both suffering from primary amenorrhea and swellings in both groins. The elder J. W. (Case 2) aged 20 was a shop assistant, while C. W. (Case 3) aged 17, worked as a maid-servant. The histories given by the two girls were similar, as were the findings on examination.

Reducible swellings had been present in both groins for as long as the patients could remember, and although these swellings increased in size on standing or exercise, they caused little inconvenience. Those on the left sides were much more marked, and J. W. (Case 2) wore a truss on this side for a few years in early life. The girls were worried because they had never menstruated although they had otherwise developed normally. There was no history of periodic enlargement of the swellings or of recurrent lower abdominal pain, and the only previous illness they both had had was infective hepatitis in 1946. Their interests and outlook were feminine, and J. W. (Case 2) had a suitor. There was nothing relevant in the family history; there was one apparently normal brother.

On examination the patients were typically feminine (Figs. 1 and 2). The breasts and external genitalia were of normal development, although the pubic and axillary hairs were soft and very scanty. Globular swellings were present in the left inguinal canals and it was possible to get above their ovoid distal portions, which lay in the axis of the canal and measured some 4 by 3 centimeters. In J. W. (Case 2) reduction was not possible at this time, but it was easily effected in C. W. (Case 3). On the right side smaller swellings appeared when the patient strained. These swellings were not tender, all of them gave a nonexpansile impulse on straining, and those that could be reduced were controlled by pressure over the internal rings. The uterus could not be felt on rectal examination. Intravenous pyelography showed normal kidneys and there were no other abnormalities on examination.

On November 12, 1948, after an initial pelvic examination under general anesthesia, the inguinal canals were explored by a single curved skin incision, and division of the external oblique aponeuroses. The findings were as follows:

In Case 2 (J. W.) the thick intact hymen was incised and the vagina found to be only 3 centimeters long. The uterus could not be felt in the pelvis. In the left inguinal region there was no evidence of a round ligament, and what proved to be the largest of the sliding hernias in this series projected through the external ring. It was defined and opened and its contents photographed (Fig. 3). The sac contained an apparently normal but smooth and retroperitoneal "ovary." Attached to its medial pole was a muscular mass which gave rise to a thin tubular structure passing with a vascular pedicle through the internal ring. Attached to its lateral pole was a clear cyst 1 centimeter in diameter suggesting a small hydrosalpinx. A pocket of peritoneum 1 centimeter deep, opened with a crescentic margin proximal to the gonad. Fimbriae were not seen, and the muscular structures faded away on being traced medially without any evidence of an intervening vesicorectal peritoneal fold. A biopsy of the gonad was taken and its brown cut-surface resembled testicular rather than ovarian tissue, while its thick, shining, smooth capsule resembled tunica albuginea rather than ovarian capsule. The sac was then closed at its neck, the remainder being everted, and its contents reduced into the abdomen with difficulty because of the narrowness of the internal ring.

Fig. 1. Case 2 (J. W.).

Fig. 2. Case 3 (C. W.).

The findings on the right side resembled those on the left but the structures were less differentiated, and the sac did not reach the external ring. The sac was closed after inspection of contents and reduced.

In Case 3 (C.W.), the thick intact hymen was incised to reveal a vagina only 2 centimeters long. The uterus could not be felt in the pelvis.

The findings on the left side were almost identical with those on the right side of J. W. (Case 2) and were dealt with in the same way.

The right inguinal canal was occupied by a normal round ligament and the smallest of the sliding hernias. Its contents resembled those of the other side but the muscular mass was not so well developed. Biopsies were taken; the muscular mass bled freely and the gonad resembled testis. Fimbriae were not seen, and the muscular bands faded away on each side of the pelvis without evidence of an intervening peritoneal fold. The hernial sac was closed at its neck, the remainder being everted and its contents reduced extraperitoneally.

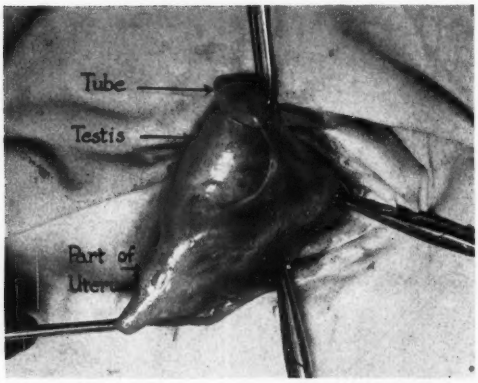

Fig. 3. Case 2 (J. W.). Contents of left inguinal canal at operation. The artery forceps are clamping the edge of the peritoneal sac.

The inguinal canals and external oblique aponeuroses were repaired with nylon, and the wound was closed with a subcuticular nylon suture. Convalescence was uneventful and the patients were discharged on the 12th postoperative day with the wounds well healed.

Biochemical investigation. In Case 2 (J. W.) the androgen excretion was 12 milligrams per 24 hours; in Case 3 (C. W.) the androgen excretion was 8 milligrams per 24 hours.

Pathological Reports

Gonad biopsies. Case 2, (J. W.), R.I.S.H. 4842/48. "Macroscopically the tissue was brown, resembling testis, with its fibrous tunica. A small piece, only, was available for study.

"The tubules, histologically, are scanty (Fig. 4). At the periphery of each tubule there is a single layer of cells of indeterminate shape with, in most cases, a deep-staining round nucleus. In some tubules these cells appear toward the center as well, and sometimes they appear to lie on acidophilic threads of tissue which form a meshwork in the tubular lumen. These are degenerate spermatogonia. About one third of the tubular cells have less regular nuclei, varying in size and shape from a little below to well above the average size, and sometimes staining less deeply than the average. These are the sustentacular cells of Sertoli. The interstitial cells are mostly large and polyhedral, with a single large round nucleus containing a fine chromatin meshwork. The cytoplasm contains much finely granular brown pigment. The stroma of the testis is provided, in addition, by unpigmented fibrocytic and fibroblastic cells. Interstitial cells are extremely plentiful, the pigmented type, or cells of Leydig, very considerably outnumbering the other types. The basement membranes of the tubules are slightly thicker than the average of a well developed functioning testis. Interstitial blood vessels are numerous and in some instances, their walls appear to be unduly thick.

"Summary: 1. The relative scarcity and complete absence of differentiation of the spermatogonia indicate a nonfunctioning testis.

"2. Interstitial hyperplasia, mainly of pigment-carrying cells of Leydig, but also of the septulae testis is present.

"3. The appearance resembles that associated with cryptorchism in an adult male, but interstitial hyperplasia is much more marked."

Gonad biopsies. Case 3, (C. W.), R.I.S.H. 4846/48. "The appearances (Fig. 5) vary from those described in Case 2 (J.W.) in that the tubules are even more sparsely distributed; that the degenerate spermatogonia at the periphery are more crowded and more regularly arranged; that the interstitial cells, although prominent, are not so markedly hyperplastic; and that the stroma is more variable in thickness and in places considerably looser.

"Summary: 1. The relative scarcity and complete absence of differentiation of the spermatogonia indicate a nonfunctioning testis.

"2. A slight degree of interstitial hyperplasia is present."

Muscular mass biopsy. Case 3, (C.W.), R.I.S.H. 4846/48. "The tissue provided suggests that it came from a structure with elements similar to those seen in a highly vascular uterus."

(We desire to thank Mr. A. Elliot-Smith for permission to publish Case 1, Dr. G. A. C. Summers, of the Department of Pathology, for pathological reports, Mr. J. R. P. O'Brien, of the Nuffield Department of Biochemistry, for androgen estimations, and Mr. E. L. P. Tugwell for the photographs.)

DISCUSSION

1. Hernias of uterus and adnexa. The whole subject of inguinal hernias of the uterus and adnexa has been fully reviewed by Meyer and Templeton (1941) and by Watson (1948). The presence of the tube with the ovary distinguishes tubo-ovarian ectopia from ovarian hernia (Donald, 1940). Tubo-ovarian ectopia is generally agreed to be present from birth, and bilateral ectopia, which is rare, is frequently associated with some other congenital abnormality.

Early treatment by replacement of the ectopic ovary is important, because it is tender in the adult, although not in the child, and it may become hypersensitive from repeated minor trauma. Cystic degeneration, torsion, strangulation, and rarely malignant change may occur, and the tube may become infected. The dangers of pregnancy in a herniated uterus, or of ectopic pregnancy in a herniated tube or ovary have been reported, and the sac may contain omentum or bowel which are

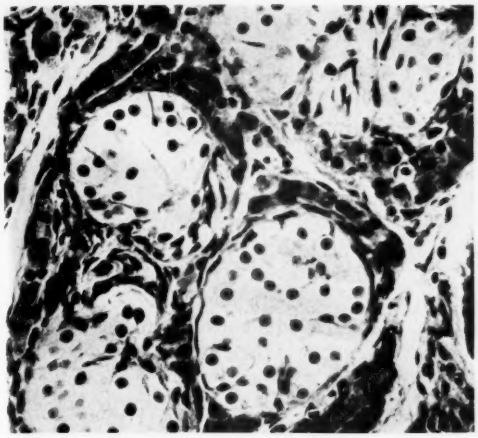

Fig. 4. Case 2 (J. W.). High power (one-sixth of an inch), of biopsy specimen, showing the increased density of interstitial cells, and atrophic tubules.

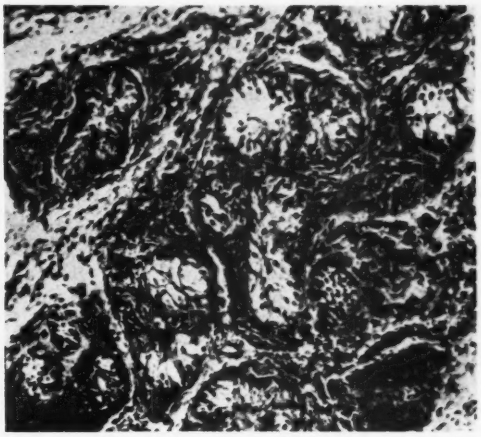

Fig. 5. Case 3 (C. W.). Low power (two-thirds of an inch), of biopsy specimen showing less advanced changes than in Figure 4.

subject to the usual complications incurred by these structures in hernias. In just over half of the cases reviewed by Watson (1948) it was necessary to sacrifice the ovary because of one or other of these complications. Finally, repair of the inguinal canal is necessary.

Ovarian hernias are generally considered to be very sensitive in adults, as are undescended testes, but tenderness was conspicuously absent in the cases now reported. Such hernias should be considered in the adult female, and the pelvic organs examined before operation, not only when the signs and symptoms of a groin swelling fluctuate with the periods (Fusaro 1946), but also when such a swelling is associated with an error of genital development.

Thomson (1948) reported a case of bilateral hernias of the uterus, tubes and ovaries, associated with absence of the vagina. He reviewed 2 cases reported by Deutschman (1923) and Stock (1944) which resembled his own, and also a somewhat similar case in a true hermaphrodite reported by Young (1937). In Case 1 it is likely that the tubular bands running medially to fuse in the midline were composed at least in part of uterine tissue. There were no globular expansions to justify the name of uterus. In the 2 other cases there seems no doubt that part of the tube and uterus was present on each side.

The ovaries develop from the genital ridge and have descended to the iliac fossae by the fifth month of fetal life, but do not reach the true pelvis until the end of the first year of life (Watson 1948). The canal of Nuck normally closes at the eighth month of fetal life. The descent of the ovaries into the inguinal canals is not fully understood. It is generally attributed to hormonal disturbances in early fetal life and to the pull of the gubernaculum in cases in which the genitoinguinal ligament fails to adhere to an undeveloped uterus and the canal of Nuck remains open. The tubes and rudimentary uterus follow. An alternative mechanism which may sometimes operate is suggested by the following case of sliding hernia of the tube:

P.W., aged 4 (R.I.No. 70038/47), was admitted for operative treatment of her left oblique inguinal hernia which had been present since birth. The large sac contained bowel, but after this had been reduced, a rounded mass 1 centimeter in diameter was felt in the medial wall of the sac. At operation this was found to be the middle part of the left tube which lay outside the peritoneum, although its fimbriated extremity and the left ovary were free in the peritoneal cavity.

If this hernia had been left to increase in size, it is probable that the remainder of the tube and then the ovary would have been dragged into the sac.

In Case 1 the ovary and tube in the right

inguinal canal lay outside the peritoneum, as does the normally descended testis; the peritoneum was seen to close at the level of the internal ring. The sliding hernia on the left side in Case 1 and on both sides of the 2 other cases, resembled an earlier stage of development in the male, where the descending testis is still associated with a congenital type of hernia. Tubo-ovarian ectopia has been said to represent the full descent of the ovary and to correspond to the descent of the testis into the scrotum. Watson (1948) considers, however, that this similarity does not exist because the testis is a retroperitoneal organ while the ovary is intra-abdominal and possesses a mesentery.

2. *Nonunion of muellerian ducts.* The paramesonephric or muellerian ducts in the female give rise to the fallopian tubes on each side, and unite to form the uterus and part of the vagina. Von Winckel (1939) suggested two possible causes preventing union of the ducts —the first, abnormal shortness of the round ligaments, (this was present in Case 1) and the second, a vesicorectal peritoneal fold (this was not found in any of the 3 cases). In the typical anomaly resulting from complete nonunion of the muellerian ducts (as illustrated by Cases 2 and 3), the upper vaginal segment is absent, and the lower vaginal segment, which is developed with the external genitalia from the urogenital sinus and the external tubercle, is seldom more than 2 to 3 centimeters deep (Wharton, 1947). Further the rudimentary tubes do not meet in the midline as in Case 1. This woman was fortunate in having a normal vagina, presumably due to fusion of at least the lowest parts of the muellerian ducts. In Cases 2 and 3 the uterine tissue on the two sides, if united, would have been sufficient to form a uterus of normal size.

Associated congenital renal abnormalities frequently occur with maldevelopment of the uterus (Counsellor, 1947) but were not present in any of these cases.

3. *Hermaphrodites.* Bland-Sutton (1920) stated that many of the glandular bodies found in the sacs of inguinal hernias of infants, apparently girls, prove to be testes when they are examined microscopically. McMillan (1942) reported a case of bilateral hernias of the gonads in a typically feminine individual. The vagina was normal, there was no evidence of a uterus, and a biopsy specimen of the gonad showed tubular structures probably of testicular origin, but the pathologist did not consider that it belonged definitely to the genitalia of either sex. Bleyer (1948) described 2 sisters in whom neither uterus nor upper vaginal segment were developed and whose gonads were proved at herniotomy to be testes. Young (1937) made a wide survey of hermaphroditism and allied conditions. A true hermaphrodite possesses the germinal cells of both sexes, irrespective of their genitalia and secondary sex characteristics; while a pseudohermaphrodite possesses the gonads of one sex but the genitalia and sometimes the secondary sex characteristics of the other. Creevy, (quoted by Young 1937), classified pseudohermaphrodites male or female depending on the nature of the gonad: and internal, external, or complete, depending on whether the internal or external genitalia, or both groups of genitalia, are of the other sex. Bland-Sutton stated that more than 95 per cent of these pseudohermaphrodites are undeveloped males. McCahey (1938) classified male pseudohermaphrodites into those with and those without muellerian remnants.

Cawadias (1946), on the other hand, considers that the conception of a true hermaphrodite or androgyne, is a remnant of ancient demonology. He prefers to classify human intersexes either male or female according to the predominant sex; and to male intersexes he gives the name androgynoids, who may be genital or gonadal in type.

The determination of sex by estimation of the urinary excretion value of androgens and estrogens is not possible because of the considerable overlap of the normal values in the two sexes. Adrenal virilism in the female, however, may often be differentiated in this way from male pseudohermaphroditism, for adrenal hypertrophy is associated with only 0.7 per cent of male pseudohermaphrodites (Neugebauer, 1908). An operation may be necessary for the final determination of sex.

Pseudohermaphroditism is not as rare as is generally supposed: Young (1937) gives the incidence as 1 in 1,000 persons. Male pseudo

hermaphroditism is often inherited, and Witschi (quoted by Allen 1939), in reviewing the literature, recorded 42 cases occurring in 11 families. The less well recognized familial incidence of female pseudohermaphroditism has recently been reviewed by our colleagues Biggs and Rose (1947).

Broster and Vines (1933) consider that male pseudohermaphroditism results from sex inversion of a chromosome sex-determined female during the first 3 months of fetal life, and that this is due to an abnormal androgenic phase of the adrenal cortex in the fetal female. The resulting gonad is functionally incomplete and unable to secrete the "inhibin" which prevents excessive gonadotrophic hormone production in the normal adolescent. They consider that the resulting greatly increased prolan production at puberty gives rise to the characteristic postpubertal testis of the pseudohermaphrodite in which the tubules atrophy and the interstitial tissue increases. In their prepubertal cases the testicular histology was not obviously abnormal for the age.

Goldzeiher and Hamblen (1947) in a careful study of 8 selected male patients, found notable discrepancies between the urinary hormone excretion, the testicular histology, and the clinical evidence of androgenic activity. They state that hypertrophy or hyperplasia of the Leydig cells cannot be regarded as indicative of increased, or even of normal secretory activity. The androgen excretion in Case 1 could be said to be at the upper limit of normal for women, and that of Cases 2 and 3, an average normal. Interstitial hyperplasia was considerable in Case 2 (aged 20) but less marked in Case 3 (aged 17); there was little evidence of androgenic activity in either case.

It seems from the histology of the gonads that Cases 2 and 3 are complete male pseudohermaphrodites, according to the Creevy classification, although it is possible that the gonads were ovotestes. This can neither be proved nor disproved without section of the complete organs.

Whether the gonads exert a masculinizing influence—in which case their ablation would lead to an increase in femininity—or whether they secrete estrin and exert a femininizing influence as suggested by Streeter (quoted by Young, 1937), or whether, if the testes are left either of these changes may occur at a later date, must depend on the individual case. Some authorities believe that mental changes follow their removal (McMillan, 1942), and Hain and Schofield (1947) point out that ablation forestalls teratomatous change. Broster and Vines (1933), Novak (1935), Ombredanne (quoted by Cawadias, 1946), Hain and Schofield (1947) and Bleyer (1948) excised the testes from intersexes who had predominantly female features and who had the desire to remain women, while Young (1937) dealing with the same problem replaced them in the abdomen. It is of interest that Ombredanne's patient subsequently developed "menopausal" symptoms unrelieved by testosterone but improved by estrogens.

Neugebauer (quoted by Young, 1937) observed that external and complete pseudohermaphrodites are most often reared in the wrong sex, and if they marry it is usually to members of their own sex. It seems natural that Cases 2 and 3 were brought up as girls, and they have had no cause to doubt their sex, although they have been told that they will neither menstruate nor reproduce. Their treatment was simpler, and the prognosis more favorable, than is the case with most pseudohermaphrodites. To all appearances they are typically feminine and, should the occasion arise, they may be allowed to marry.

It is interesting to speculate on the histology of the gonads of Case 1, the contents of whose inguinal canals, except for the well developed round ligaments, resembled so closely those of the 2 other patients. It is possible that she, and at least some of the similar cases that are from time to time encountered, are in reality further examples of complete male pseudohermaphroditism.

SUMMARY

1. Three cases of bilateral hernias in apparent females, associated with primary amenorrhea and absence of uterus, are described.

2. All the hernias contained gonadal structures.

3. In each case, operation was necessary for the cure of the hernias and was not primarily undertaken to determine sex.

4. Biopsy examination revealed the presence of testicular tissue in two "sisters," aged 17 and 20. These gonads were not removed because secondary sex characteristics were relatively well developed and it was considered that there must be some female gonadal activity.

5. The importance of a thorough pelvic examination of women with inguinal hernias is stressed.

6. The literature of hernias of the uterus and its adnexa, of nonunion of the muellerian ducts, and of male pseudohermaphroditism, is briefly reviewed.

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THE USE OF CAPSULECTOMY AND ARTHROPLASTY FOR LIMITATION OF FINGER MOTION

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THE treatment of ankylosis of finger joints always has been a major problem for the medical profession. In the past, disability to the patient has been great and the results of treatment have been poor. Because of the large number of such disabilities incurred in World War II a concentrated effort was made in the field of treatment and now in civilian life it is possible to improve, or to restore motion at the finger joints completely. Whenever the limit of conservative treatment is reached and disabling deformity of the fingers still remains, surgery is indicated.

The literature concerning the subject is limited to 21 publications, 9 of which are foreign. With very few exceptions the experience of each author is limited to 1 or 2 cases of arthroplasty, and emphasis is placed upon the type of tissue interposed between the reconstructed bones. The number of cases recorded, the joint operated upon, and the type of material used are indicated in the following: arthroplasty of two interphalangeal joints with periosteum from the tibia as interposition material (11); arthroplasty of one finger joint with a free fat transplant (19); 2 of the thumb with a piece of capsule (18); of an interphalangeal joint with the method not described (6); 2 of metacarpophalangeal joints with a free flap of fat plus fascia (9); and 1 with fascia only (4); a collection of 90 cases performed by various surgeons throughout the Russian Army during World War I in which interposed fascia was considered more successful than fat or capsule (20); 1 of an interphalangeal joint with a thin flap of subcutaneous fatty tissue (15); and 1 with fascia lata (1); 14 of finger joints with periosteum or fascia (10); 1 of the carpometacarpal joint of the thumb with fascia (17); and 1 with a double flap of fascia lata (14); several of the metacarpophalangeal joints with flaps of connective tissue taken from adjacent parts (12); 1 each of a metacarpophalangeal and an interphalangeal joint with fascia from the thigh (16); and 1 each with a vitallium cap (3); 2 of the metacarpophalangeal joints with tunica vaginalis (21); several of the metacarpophalangeal joints with slippery fascia from the elbow or knee (2); 2 cases of excision of the metacarpal heads for rheumatoid arthritis without the use of interposition material (13); 16 of the metacarpophalangeal joints with the fine fascia which overlays the fascia lata (5); and 6 of the metacarpal heads with the fourth or fifth metatarsal bones (7).

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CAPSULECTOMY

The term capsulectomy denotes the removal of the collateral ligament on both sides of an interphalangeal or metacarpophalangeal joint. The ligament is an obliquely situated, short, round, thick band which firmly connects the bones of the joint (Fig. 2). It is tense in all positions of the joint and particularly in flexion because of the greater radius of curvature of the volar aspect of the head of the bone. Removal of the ligament, therefore, allows further flexion to occur.

The operation is useful when ankylosis is the result of prolonged immobilization, disuse, and contracture not due to bony destruction, arthritis, trauma, or fixation of the flexor or the extensor tendons. An excellent indication for the operation is present whenever the roentgenograms reveal the cartilage space of the ankylosed joint to be preserved. The procedure may be performed on one or more fingers, at any joint, and on more than one joint of the same finger.

The operation is performed by making a 2 centimeter longitudinal incision on the posterolateral and the posteromedial aspects of the joint. The digital nerve and artery are pro-

Figs. 1 to 4. Capsulectomy.
Fig. 1, above. Roentgenograms showing compound fractures of second, third, and fourth metacarpal bones resulting in ankylosis of corresponding metacarpophalangeal joints at 180 degrees.

tected and the tendon of the interosseous muscle is retracted. The collateral ligament is seen to extend from the posterior aspect of the proximal bone to the anterior aspect of the adjacent distal bone. The ligament is incised flush with each insertion and removed completely. Should passive motion of the joint be less than expected the anterior capsule is explored and if found to be adherent to the

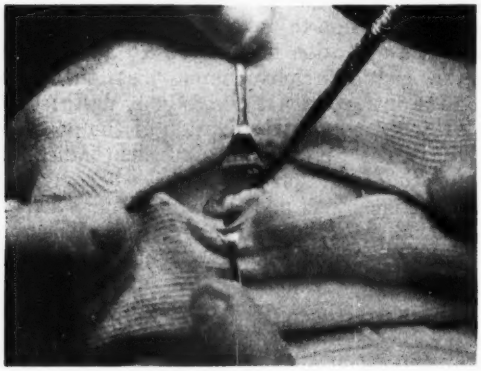

Fig. 2. View showing one of the collateral ligaments before incision.

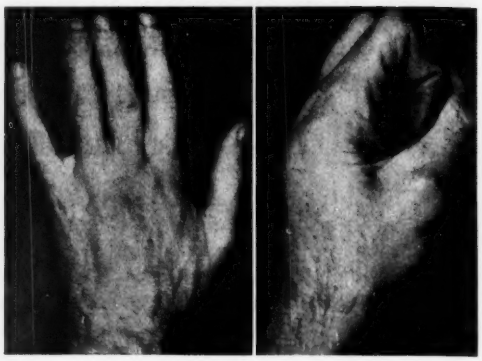

Fig. 3, left. View showing degree of extension of second, third, and fourth fingers 9 months after operation.
Fig. 4. View showing degree of flexion of second, third, and fourth fingers 9 months after operation.

bones, it is freed by blunt dissection. However, the capsule of the joint must not be incised, particularly transversely, because the degree of motion gained is minimal, the joint will subluxate, and after healing the degree of ankylosis often is greater than before operation. Upon closure very few subcutaneous sutures are used because of the thinness of the tissues. The skin is united by interrupted vertical mattress No. 0000 silk sutures. A dry dressing is applied with the fingers in firm flexion, but no splint is used.

Postoperative care consists of movement of the finger daily by the surgeon until the third day at which time the patient begins to perform passive and active motion four times daily.

The degree of improvement varies with each patient. Upon the completion of the operation motion is greater than later and one can anticipate a gradual loss of about 20 degrees, but still there will be a permanent increase in motion ranging from a minimum of 30 degrees to a maximum of 90 degrees. Less improvement occurs at the proximal and distal interphalangeal joints.

In the case illustrated the patient suffered a compound infected fracture of the second, third, and fourth metacarpal bones (Fig. 1). After long immobilization the corresponding metacarpophalangeal joints were ankylosed at 180 degrees, so that the ability to grip with the hand was completely eliminated. Cap-

Fig. 5, above. Roentgenograms of third finger before operation.

Fig. 6. Roentgenograms of the third finger after operation had been performed.

Figs. 5 to 7. Arthroplasty with resection of metacarpal head.

sulectomy was performed at the ankylosed second, third, and fourth metacarpophalangeal joints (Fig. 2). Nine months later extension was normal (Fig. 3), and active flexion of at least 30 degrees was present in the previously ankylosed three joints (Fig. 4). Although flexion is not normal the picture reveals that the patient is able to grip which is of great value when it is considered that before capsulectomy the patient had a relatively useless, claw-like hand with no grip possible. It is obvious that the operation gives even better results in a hand with less deformity. However, should the degree of increased motion after operation appear to be small it must be remembered that while motion of a few degrees is of no value in a joint of the lower extremity motion of a few degrees in the joints of the fingers is extremely valuable, and often the difference between a useful and a disabled hand.

ARTHROPLASTY

The term arthroplasty denotes the removal of the base of a proximal phalanx or the head of a metacarpal bone. The operation should be performed for limited motion at a metacarpophalangeal joint whenever the cartilage space is decreased or destroyed because of arthritis, fracture, or traumatic disruption (Figs. 5 and 8) provided the skin is loose and the soft tissues are in good condition. The metacarpal head (Fig. 6) or the proximal 1 centimeter of the proximal phalanx (Fig. 9) is resected depending upon which is deformed or which shows the greatest involvement. The procedure should not be used for ankylosis of the interphalangeal joints. It is rarely successful at the proximal interphalangeal joint because of posterior subluxation and lateral instability, and it should never be tried at the distal interphalangeal joint.

A 4 centimeter longitudinal incision is made on either side of the posterior aspect of the metacarpophalangeal joint. The subcutaneous tissues are incised, the extensor digitorum communis tendon is retracted to one side and the interosseous tendon to the other side. The

Fig. 7. View showing degree of flexion of third finger 27 months after operation.

Fig. 8, above. Roentgenograms of third finger before operation.

Fig. 9. Roentgenograms of the third finger after operation had been performed.

Figs. 8 to 10. Arthroplasty with resection of phalanx.

capsule of the metacarpophalangeal joint is incised longitudinally. The deformed metacarpal head or the proximal 1 centimeter of the proximal phalanx is removed by mallet and osteotome. The rough bone edges are smoothed down by rasp and all scar tissue, adhesions, and irregular surfaces are removed; however, any remaining articular cartilage on the opposite bone is preserved. Through a 4 centimeter longitudinal incision over the posterior aspect of the upper one-sixth of the ulna a 4 by 4 centimeter piece of slippery fascia is removed and the incision closed. The slippery fascia is applied to the distal extremity of the metacarpal bone irrespective of whether the metacarpal head or the proximal portion of the proximal phalanx has been removed. It is placed over the metacarpal bone and beneath the tendons in the form of a cap with the slippery surface facing externally or toward the joint and is sutured to the surrounding periosteum by interrupted No. 0000 black silk sutures. If a tourniquet has been used it is removed at this time and all bleeding points are ligated. The capsule is united by interrupted No. 0000 black silk sutures as are the subcutaneous tissues, and the skin is closed by interrupted vertical mattress sutures. A dry dressing is applied with the finger flexed to an angle of 90 degrees. Traction to the finger is not necessary.

Fig. 10. View showing degree of flexion of third finger 5 months after operation.

The results of arthroplasty of the metacarpophalangeal joints are good (Figs. 7 and 10). One can anticipate 30 to 70 degrees' additional motion. Some authors deny the use of interposing material, but it is thought that Bunnell is correct in stating that slippery fascia should be used to protect the raw bony surfaces. The

procedure is of unusual value in ankylosis of the metacarpophalangeal joints due to arthritis.

SUMMARY

1. Capsulectomy and arthroplasty for limitation of finger motion have been discussed from the experience gained in 13 cases.

2. Indications and contraindications for each procedure have been given.

3. The details of the operative techniques have been recorded.

4. The degree of improvement which can be anticipated has been specified.

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EXPERIENCES WITH CARDIAC ARREST

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THE first death attributed to anesthesia occurred on January 28, 1848 (6). This was a little more than a year after the introduction of ether anesthesia and about 2 months after the introduction of chloroform in obstetrical anesthesia. There were enough reported facts about this first death under anesthesia, which incidentally was an ether anesthetic, to make one feel it may have been a cardiac arrest. One hundred years later the problem of cardiac arrest is still present and, if anything, is more pressing than ever.

Barber and Madden, in a consideration of the historical aspects of cardiac resuscitation, pointed out that the earliest reports on manual massage for cardiac resuscitation were the experimental studies of Schiff in 1874. Work on dogs and rabbits appeared at intervals from 1898, when Tuffier and Hallion confirmed the work of Schiff, until 1903. These reports seemed to indicate an ability of cardiac massage, of an electrical current, and of Locke's solution injected into the coronary arteries frequently to restore the heart beat of dogs and rabbits. Niehaus, in 1889, first attempted cardiac resuscitation by manual massage, but was unsuccessful. Maaj, in 1900, was the first to report a partial success. He was able to reestablish cardiac pulsations and spontaneous respirations for 11 hours. Ingelsbrid, in 1901, first succeeded in resuscitating the heart but it was not reported until 1904. Starling and Lane, in 1902, first reported a successful case of resuscitation of the human heart using subdiaphragmatic massage. Barber and Madden reviewed the literature to 1945 and found that 143 cases of cardiac arrest had been reported. This small number of cases from 1848 to 1945 makes the incidence of cardiac arrest appear to be very low. If the reported cases give an accurate idea of the relative frequency of this complication in former years, then something has happened in recent years to make cardiac arrest occur more frequently. The probability is that this is not the case but that we are all now more aware of the possible occurrence of this condition and that more anesthetists and surgeons are on the lookout for it than previously.

Our own experience and conversation with, and letters from, men in all sections of the country reveal an increased frequency and, consequently, an increased consciousness of this problem. This is an emergency requiring prompt decisions, radical treatment and a knowledge of the very short time available in which to bring about a successful outcome. It is important to realize that cardiac arrest, while infrequent, is by no means a rare complication and is one which, to make life-saving possible, requires instant planned action, without which the heart will all too frequently be restored to action but unfortunately at a time when mental deterioration has already taken place.

The expectancy of death during operation and anesthesia from all causes is 1 to 1,000 in a large number of cases in five teaching hospitals in three continents. The expectancy for cardiac arrest is undetermined but much less. The important point to remember, however, in cardiac arrest is that in the past many have been lost who could have been saved (10).

INCIDENCE

In the past 7 years there have been 13 cases of cardiac arrest in the Lahey Clinic operating rooms. Bailey, who has had an extensive experience with this problem, has apparently had about 2 cases a year. This concurs with others' experiences and our incidence. We may assume that in a busy operating room suite 1 to 2 cases may be expected per year, and we must assume that whether these patients live or die is based upon how well the operating personnel is organized to deal with the instances which occur.

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DIAGNOSIS

The surgeon is not usually the first to establish a diagnosis in this complication unless the operation he is doing is of such character that he happens to have an artery under direct vision and notes cessation of pulsation in it, or the chest is open and the heart or large vessels are visible. The anesthesiologist is most frequently the first to become aware of sudden cardiac arrest, and it is he who in a great majority of cases will need to notify the surgeon of the need for immediate action. A constantly alert watch of the patient must be maintained for this condition by both the anesthetist and surgeon since cardiac arrest may occur at any time during the induction and maintenance of the anesthesia and at any stage of the operative procedure. The type of operation performed is of no assistance in anticipating or preventing sudden cardiac arrest since it may occur during any type of operative procedure. It may also occur with any anesthetic agent or combination of agents. This includes spinal anesthesia when used as the sole anesthetic agent. In our group of 13 cases the ages of the patients ranged from 7 to 65 years. There were 8 males and 5 females. Premedication consisted of 1/6 grain of morphine sulfate and ⅓ grain of pantopon plus 1/150 grain of scopolamine and 1½ grains of nembutal. Cardiac arrest occurred during the following operative procedures: chest operation, 3 cases; abdominal operation, 4 cases; thyroid operation, 2 cases; sympathectomy, 1 case; brain operation, 1 case, laryngoscopy, 1 case; induction, 1 case.

The anesthesiologist must notify the surgeon as soon as the pulse and blood pressure disappear. If he even suspects that there has been a cardiac arrest, the surgeon must be asked to check arterial pulsations. False alarms will inevitably occur but must be understandingly tolerated. The short time during which treatment, to be effective (3½ minutes), must be applied means that the anesthesiologist and surgeon cannot waste time in useless checking, but must be ready for instant decision and rapid preparation for emergency measures.

Equipment for the management of these cases, needle and instruments already sterilized, and drugs should be at hand ready for use at all times in the operating room. Without this forehandedness the time loss and the inevitable confusion will result in restoration of cardiac activity too late to retain full and normal cerebration. If this paper does nothing more than to prompt surgeons to be aware of the possibility of this complication and be prepared for it, it will have been worth writing.

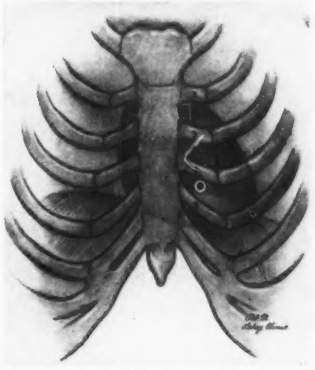

Fig. 1. The point at which the needle is inserted for the intracardiac injection is shown by the black dot. The plunger of the needle must be withdrawn so that the syringe fills with blood to demonstrate that its point is within the ventricle. If it becomes necessary to open the chest to accomplish manual massage, the incision is best made in the fourth interspace, cross-cutting its sternal cartilage in order to make room for the hand.

ETIOLOGIC FACTORS

There are few instances in which the causation of cardiac arrest may be definitely ascertained. Several factors of possible etiologic significance are known. Any one or all of these may play a part in precipitating this emergency. There are certainly other factors which we do not know of at present and which probably play a part in sudden cardiac arrest. The ability of chloroform, cyclopropane, and ethyl chloride (17) to sensitize the heart to the action of epinephrine is well known. Hypoxia (7) sensitizes the heart and causes an increased content of epinephrine in the circulating blood. Excitement causes an increased epinephrine content in the blood. Hypoxia(9) may sensitize the carotid sinus with a resultant reaction to stimulation of the carotid sinus, producing inhibition of cardiac activity. Intravenous barbiturates (8) and cyclopro-

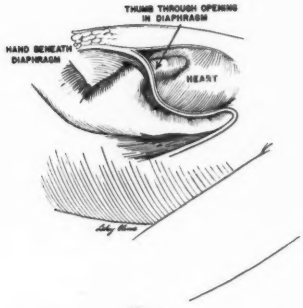

Fig. 2.

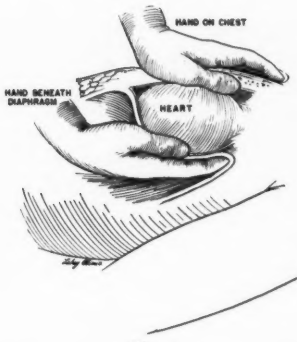

Fig. 3.

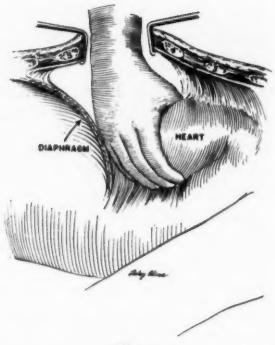

Fig. 4.

Fig. 2. The plan of incising the diaphragm is illustrated. One thumb grasps the heart in front and the fingers below through the diaphragm grasp it in back.

Fig. 3. In this illustration is shown the method of massaging the heart through the diaphragm with counterpressure on the chest by pushing the heart against the chest wall and sternum. It is usually not possible to obtain the degree of compression shown. This is a doubtful method in terms of effectual cardiac massage.

Fig. 4. In this illustration is shown the incision between the fourth and fifth ribs and the hand above the diaphragm grasping the heart in order to carry out direct compression of the heart. This is the most effectual method of maintaining circulation when prolonged cardiac arrest has occurred.

pane have a parasympathetic effect on the heart. Stimulation of the vagus nerve may inhibit cardiac activity(16). There may be a sensitivity to a drug as when sudden cardiac arrest occurs under spinal anesthesia alone. Too deep anesthesia causes sudden simultaneous cardiac and respiratory arrest. This list of possible causes is undoubtedly incomplete but it furnishes the basis for the plan of treatment for this complication.

Having personally participated in some of these cases, both of us are conscious of how disquieting they are, how difficult it is for surgeon, anesthetist, and particularly for the other operating room personnel to act and function effectively without panic and without undue loss of time. We have learned from our experiences that 3½ minutes, the limit of time available, is too short to trust to anything but planned, prepared, and practiced effort. If one depends upon improvisations such is the dramatic nature of the situation that excitement and panic instead of calm and logical steps will dominate it. What is needed is a definite practiced plan of action, the only way by which the necessary time can be preserved to save, not life, but particularly the intellect. In all of these cases it has been possible to restore cardiac action but in some so late that cerebral damage has occurred and the patients have died a few days after operation.

TREATMENT

Weinberger, Gibbon, and Gibbon have demonstrated experimentally that treatment must begin within 3½ minutes of cessation of circulation of blood. These workers showed that interruption of circulation to the brain for 3½ minutes or longer resulted in permanent changes in psychic behavior. Interruption for 8 minutes and 45 seconds was incompatible with life for more than a few hours. Unfortunately, this work is all too well borne out by our and others' clinical experiences.

A plan of action which we have presented before and see no reason as yet to change is suggested. It may be wise to post some plan of action in every operating room. It consists of: (1) artificial respiration with 100 per cent oxygen; (2) immediate cardiac massage by the surgeon—this is the all important step; (3) drug therapy consisting of the use of procaine and epinephrine; and (4) general methods of treatment including the administration of intravenous fluids and the institution of 5 to 10 degree Trendelenburg position.

When procaine and epinephrine are on the instrument table it is good practice to do a cardiac puncture, aspirate blood, and inject the solution before beginning the steps of cardiac massage (Fig. 1). This step has value since we believe some hearts showing clinical signs of cardiac arrest are not actually arrested.

This step should *not* be included in the treatment if the sterile syringes and solutions are not ready for instant use since their procurement will result in a fatal loss of time.

Artificial respiration with 100 per cent oxygen presupposes an unobstructed airway. An endotracheal tube should be inserted if it is not already in use. This can be done by anesthetists expert in their use while other measures are being carried on. Artificial respiration maintains a high concentration of oxygen in the alveoli and also has some mechanical effect in maintaining a slight circulation of the blood. Artificial respiration may need to be continued from a few minutes to several hours after the reappearance of cardiac activity. Return of cardiac activity does not always signal immediate return of respiratory activity.

Artificial respiration alone is insufficient and is useless unless the circulation is maintained. In cardiac arrest this portion of the treatment must be undertaken by the surgeon. Cardiac massage is the all important factor of the treatment and must be started without delay if a favorable outcome is hoped for. The approach to the heart depends on the operative procedure in which the arrest occurs but resolves itself into three routes: (1) transperitoneal subdiaphragmatic; (2) transperitoneal transdiaphragmatic; and (3) transthoracic.

The rate of cardiac massage has been quoted at various figures. Nicholson recommended 80 compressions per minute. There have been many guesses but Gunn has offered a really plausible rate with an explanation for his statement. He maintained that massage of the heart is not a question for indifference but that attention to detail is important. He even suggested practice for this maneuver. Gunn stated that compression should be gradual and relaxation abrupt with rate of compression at most only half the normal rate. The massage must be interrupted at regular short intervals for a few seconds in order to allow spontaneous beats to develop. The lower than normal rate of compression was recommended in order to allow the ventricles to fill and because it is a subnormal rate of beat that one is attempting to elicit, namely, the rate at which the arrested heart would start beating again. A prompt return of heart beat probably is the result of massage plus epinephrine. Gunn has emphasized that massage is used to stimulate the heart and maintain circulation and that the most important thing is stimulation of the heart. In the excitement of the moment mechanical stimulation of the heart can be overdone. One should frequently stop and watch for the first feeble heart beats. If these do not improve, then help must be supplied at intervals, and it is here that epinephrine may frequently be of great aid (Figs. 2, 3, 4, and 5).

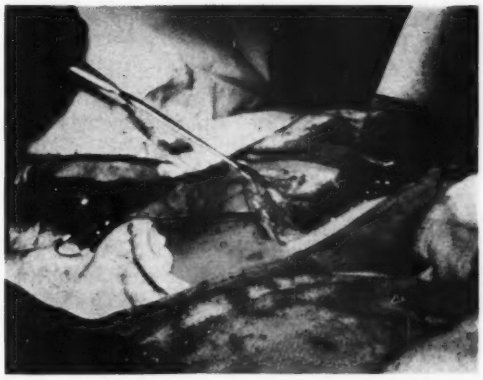

Fig. 5. Photograph taken at operation showing actual cardiac massage through the fourth interspace, as shown diagrammatically in Figure 4.

It has been noted sometimes that with the first attempts at respiration the heart occasionally stops permanently when it has had only faint flickers of action. The possible cause is a return of respiratory activity, signifying a return of other medullary centers to action. There may then be a sudden burst of vagus activity with cessation of heart beat. This is one of the reasons in the treatment of this condition for combining procaine with the epinephrine since it aids in offering protection against this complication.

Gunn has demonstrated quite positively the effectiveness of cardiac massage in animals. A dye injected into the right ventricle of an arrested heart of a dog appeared in the lungs and carotid artery after a few compressions of the heart.

To facilitate the prompt application of cardiac massage, instruments for opening the abdomen and chest should be available for use

at all times in the operating room in a specially labeled container.

In our experience (18), procaine and epinephrine appear to have been of real value in treating cardiac arrest. Epinephrine has been a time-honored favorite in any circulatory emergency. Its indiscriminate use, with its ability to produce ventricular fibrillation is, however, always unwise. Bailey, who has had a large experience with cardiac arrest, has stated that he has never seen epinephrine alone revive a heart which has already stopped but that it will increase the force of contractions in decided enfeeblement of the heart. This is in agreement with our experience with its use in cardiac arrest. We have more than once under direct vision seen a heart beating but with no palpable pulse or audible blood pressure and we feel certain that some of the seemingly cardiac arrest cases may be of this nature. For this reason, we do not hesitate when a presumed cardiac arrest occurs to administer epinephrine in small dosage combined *with* procaine. This has been done with full awareness of the propensity of epinephrine to cause arrhythmias and possibly ventricular fibrillation. This procedure has been followed in every one of our cases and while in some cardiac action has been restored too late to preserve normal cerebration and life, in every patient the cardiac beat has been restored.

Procaine given intravenously is of real value in handling patients who develop cardiac arrhythmias during thoracic surgery. The topical use of procaine is also effective in treating ventricular fibrillation. The intravenous and topical use of procaine now seems soundly established as a means of treating cardiac irregularity and sudden cardiac arrest.

We would like to re-emphasize the fact that the true value of drug therapy in cardiac arrest is to intensify the effect of the real mainstay of the treatment of this condition, that is, cardiac massage. Since we have become more keenly interested in trying to save more patients with cardiac arrest it has been our practice to have in the operating rooms, ready and mixed, 0.5 cubic centimeter of epinephrine 1:1000 and 9.5 cubic centimeters of procaine, 1 per cent, so that both drugs may be administered in a single injection.

When the diagnosis of cardiac arrest is made, an injection of the 10 cubic centimeters of the already mixed and available procaine and epinephrine is done by the quickest and most easily accessible intravenous route. If a choice of intravenous routes is possible, an antecubital vein is preferred since it is closer to the heart than is a leg vein. Age and debilitation may be factors in causing one to administer only 5 cubic centimeters of this solution. If the heart has not resumed activity soon after cardiac massage has begun, the next 5 cubic centimeters may be injected directly into the heart, preferably the cavity of the right auricle or ventricle, the needle being inserted directly into the cavity and its position proved by the ability of the surgeon to withdraw blood freely into the barrel of the syringe. The barrel containing the solution is then connected and the material introduced.

Following this procedure, if cardiac activity is slow in returning, it is probably wise to omit the epinephrine until there is some return of automatic cardiac activity, but procaine should be repeated or kept running in a continuous intravenous drip until regular cardiac action is restored.

Many other drugs (20) have been used in these emergencies. There is little reason to use a great number of these agents. Restriction of use of a variety of drugs enables one better to evaluate the efficacy of the two which, by experience, appear to have given the most reason for their use.

RESULTS

The cases collected by Barber and Madden numbered 143. Forty-eight of these patients, or 33 per cent, were treated with complete success. Bailey had a personal experience with 40 cases of cardiac arrest. He was able to revive 13 patients and of these, 4 survived. We have now had 13 cases of cardiac arrest, cardiac action has been restored in every case but only in 5 cases, or 38 per cent, has there been recovery with normal mentality. One other patient recovered, with normal mentality but died on the second postoperative day from acute cardiac failure, this case is not included in the 5 successful cases.

COMPLICATIONS

Ventricular fibrillation (13) is reported in the literature to be the most frequent complication of cardiac resuscitation and when it occurs it must, of course, be treated promptly. We have not seen it occur in any of our cases and feel that the possible reason may be the employment of procaine in the initial treatment. When the heart is under direct vision and fibrillary cardiac movements are preserved, Beck recommended the use of cardiac massage first. If unsuccessful, he advocated the injection of 5 cubic centimeters of 2 per cent procaine into the cavity of the right heart and continuation of cardiac massage. Beck has also stated that procaine, 5 per cent, or "metycaine hydrochloride" (*New and Nonofficial Remedies*), 10 per cent, applied to the surface of the fibrillating ventricle may be effective in augmenting heart action. This elevates the threshold of cardiac muscle to incoming stimuli and renders ineffective the minimal stimulus producing the fibrillation.

Beck has also used the electrical countershock method in treating ventricular fibrillation. Two padded silver electrodes, 25 square centimeters in size, are moistened in sterile isotonic solution of sodium chloride and applied to the anterior and posterior surfaces of the heart. An electrical current of 1 to 1.5 amperes through a 60 cycle alternating current is applied for 0.1 to 0.5 second. The heart muscle is contracted and brought to a standstill. Then a normal rhythm may be renewed. Should the first shock fail, manual massage is resumed, procaine is injected as previously recommended, and the shock repeated. If failure still results, Beck recommended the use of 1 cubic centimeter of epinephrine, 1:1000, or 5 cubic centimeters of calcium chloride, 1 per cent, to be injected into the right ventricle to increase its tone and elasticity. The shock is again repeated and, it is stated by Beck, the fibrillation is usually overcome. Electrical countershock therapy, while experimentally interesting, is clinically impractical in most cases in which these emergencies occur.

PATHOLOGY

Revival of cardiac and respiratory activity even to the levels existing prior to the cardiac arrest does not signify assurance that these patients will survive. These patients often die in the period of 1 to 15 days postoperatively. During this time many of them show every sign of marked damages to the central nervous system (especially those with cerebral damage). The sensitive cerebral cortex cells are first affected by interruption of the circulation, with resultant ischemia and anoxia. It is not usual to find demonstrable macroscopic or microscopic evidence of damage to the brain in these cases. In the heart itself often the only gross pathologic changes seen are the result of rough or forceful cardiac massage. It is not rare to find a hemopericardium following blind intracardiac injections. With these demonstrated findings in mind it is important to remember the need for gentleness and care in attempts to restore cardiac action.

In 1946, Hawkins, McLaughlin, and Daniel reported the case of a patient who died 26 days following cardiac arrest of 10 to 11 minutes while in the operating room. They found degeneration of the cerebral and basal ganglions. Microscopically, there was disappearance of most of the pyramidal cells of the cerebral cortex and an increase in astrocytes and microglial proliferation, especially in the occipital cortex. Chromatolysis was evident in the few surviving cells. Destruction of the occipital cortex and superior temporal gyrus was severe. Blood vessels were not abnormal; there was no thrombosis or perivascular hemorrhage.

REPORT OF CASES

CASE 1. The cardiac arrest in the reported case of pulmonary lobectomy by Adams and Hand from this clinic occurred in a man, aged 20 years, 2 hours after the start of cyclopropane-oxygen anesthesia when a suction catheter was introduced into the trachea by way of the endotracheal tube. The patient gave three convulsive coughs, and cardiac and respiratory activity ceased. This was, of course, plainly visible as the chest was open and the heart exposed. This patient was treated with cardiac massage supported by drug therapy. This case strengthened the belief that cardiac massage was the mainstay of the treatment for cardiac arrest. It was also felt then that drug therapy was of assistance but only if specific drugs could be found. Procaine was thought to be one of these drugs. This case apparently fits in well with those instances of cardiac arrest which can be traced to a vagovagal reflex.

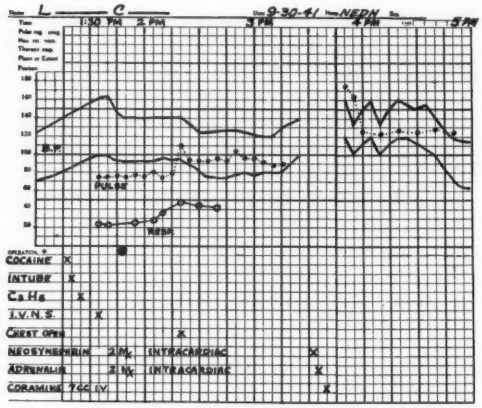

Fig. 6. Anesthesia chart. This is the first case of cardiac arrest. Since lobectomy was being performed, the chest was open and manual cardiac massage was done for 20 minutes.

This the first case of this series resulted in complete recovery (Fig. 6).

CASE 2. A woman, aged 35 years, was undergoing hysterectomy following dilatation and curettage. When a clamp was placed on the uterus, sudden cardiac arrest occurred. This was 30 minutes after induction of spinal anesthesia with 17 milligrams of tetracaine hydrochloride and dextrose solution and 10 minutes after the intravenous administration of morphine sulfate, 1/6 grain (10 mgm.), and scopolamine, 1/150 grain (0.4 mgm.). Artificial respiration by manual pressure on the breathing bag was begun immediately, as was transperitoneal subdiaphragmatic cardiac massage. One cubic centimeter of 1 to 1,000 epinephrine solution was also given intracardially. In about 5 minutes heart action had returned; respirations returned 20 minutes later. The operation was terminated. After operation, for 48 hours the patient had hyperirritable reflexes with a Babinski reflex. Reflexes became normal, and the patient made an uneventful recovery except for a loss of memory for events of the 24 hours before operation.

CASE 3. A man, aged 31 years, undergoing cholecystectomy, had cardiac arrest 30 minutes after induction of spinal anesthesia with 18 milligrams of tetracaine hydrochloride and dextrose solution and 20 minutes after the operation was begun, while the cystic duct was being exposed. An endotracheal tube was introduced and artificial respiration begun. Subdiaphragmatic cardiac massage was carried out for a few minutes. Then an incision was made in the dome of the diaphragm and transdiaphragmatic cardiac massage was carried on. Cardiac activity reappeared in about 15 minutes. The operation was completed rapidly.

Seven hours after operation the patient was unconscious, hyperventilating, and showing hypertonic rigidity and carpopedal spasm. In 2 days he exhibited a flaccid paralysis. On the fifth day tracheotomy was done because of the respiratory obstruction which a flaccid epiglottis created. The temperature remained high, cord bladder developed, and the patient died on the fifteenth day.

The abnormalities noted at necropsy were inconclusive. There was slight cerebellar coning from pressure and terminal bronchopneumonia. Microscopic sections revealed diffuse slight edema and slight gliosis. Cause of death not determined pathologically.

CASE 4. A woman, aged 44 years, undergoing splanchnicectomy for essential hypertension, had cardiac arrest after a few warning signs, which is unusual. Twenty-five minutes after induction of spinal anesthesia with 20 milligrams of tetracaine hydrochloride and dextrose solution, during which time the patient received 0.2 milligram of pentothal sodium (*N. N. R.*), and 15 minutes after the operation was begun, the surgeon had exposed the lumbar sympathetic chain, when the patient was noted to be cyanotic around the lips and using her accessory muscles of respiration. Administration of oxygen by manual positive pressure was of no help, and cardiac and respiratory arrest occurred suddenly.

The patient was placed on her back and intubated; artificial respiration was begun and epinephrine, 0.5 cubic centimeter, was injected intracardially. In 3 minutes heart sounds were heard, but no pulse or blood pressure was elicited for another 30 minutes. The operation was immediately terminated. Although the patient looked well oxygenated and showed no unusual signs, she never regained consciousness and died on the third postoperative day.

Postmortem examination did not reveal damage to the brain grossly or microscopically. Pulmonary atelectasis, hydrothorax on the left side, pulmonary congestion and edema, laceration of a coronary vein with hemopericardium of 300 cubic centimeters, myocardial hypertrophy and dilatation were present. The immediate cause of death was anoxemia according to the report of the pathologist. It is likely that this patient had a complete or total spinal anesthesia preceding the anoxemia.

CASE 5. A man, aged 47 years was undergoing division of a sensory root for trigeminal neuralgia when he suddenly took two deep breaths, and cardiac and respiratory activity ceased. This occurred while the fibers of the second and third divisions of the trigeminal nerve were being divided. The patient was placed supine and artificial respiration begun. About 12 minutes later an incision in the upper part of the abdomen was made and subdiaphragmatic cardiac massage begun. Epinephrine, 0.75 cubic centimeter intramuscularly, produced no change. Epinephrine, 0.5 cubic centimeter, was injected into the heart while massage was continued. On piercing the heart muscle with the needle a few spontaneous movements were felt. Cardiac activity was resumed after an arrest of about 20 minutes. The operation was terminated.

In 1 hour the patient reacted to painful stimulation and groaned. He exhibited hypertonicity of all

extremities and, at times, a coarse tremor. Bilateral pneumothorax developed, and 1,300 cubic centimeters of air were removed from the left side of the chest. He never regained consciousness and died on the seventh postoperative day. The supervising anesthesiologist felt that this patient may have reached the fourth stage of ether anesthesia when cardiac and respiratory arrest occurred.

Postmortem examination did not reveal gross or microscopic damage to the brain. There was confluent bronchopneumonia, which was called the immediate cause of death. Too much time was lost in getting patient out of an upright position chair in which the sensory root division was done.

CASE 6. A man, aged 65 years, was undergoing a thyroidectomy when cardiac arrest occurred while the anterior edge of the sternomastoid muscle was being freed. This was 20 minutes after induction of anesthesia with ethylene-oxygen and subsequent anesthesia with ether-oxygen, and 5 minutes after the operation was begun.

Artificial respiration was immediately begun, and 1 cubic centimeter of 1 to 1,000 solution of epinephrine was given intravenously. In 10 minutes cardiac and respiratory activity appeared as before operation. The operation was then completed. The postoperative course was normal on the first day. On the second day patient conversed with a visiting physician and then suddenly died. He was a known cardiac cripple who had long had treatment for cardiac decompensation and hyperthyroidism before operation. The episode in the operating room may have been the evidence of a hypersensitive carotid sinus.

Postmortem examination of the brain did not reveal damage grossly or microscopically. Cardiac dilatation, mitral stenosis, and arteriosclerosis were noted; cardiac failure given as the immediate cause of death.

CASE 7. A man, aged 30 years, was undergoing a gastric resection. Cardiac arrest occurred suddenly when the right gastric artery was clamped. This was 30 minutes after induction of spinal anesthesia with 18 milligrams of tetracaine hydrochloride and dextrose solution and 0.4 gram of sodium pentothal (*N. N. R.*). Morphine sulfate, 1/6 grain (10 mgm.), was given intravenously about 30 minutes before the cardiac arrest.

Subdiaphragmatic cardiac massage was begun, and 2 cubic centimeters of epinephrine, 1 to 1,000 was injected into the heart. A tube was placed in the trachea and artificial respiration begun. In about 10 minutes pulse became palpable at a rapid rate, 20 minutes later respirations returned.

Postoperatively, the patient had convulsions and tonic contractions of the extremities lasting 4 minutes at a time. On the second day he became flaccid and had no more convulsions. The temperature remained high and the patient died on the third day. Permission for autopsy could not be obtained.

CASE 8. A man, aged 49 years, was admitted to the hospital for biopsy of a suspected carcinoma of the vocal cord. He was short, obese, and had a history of drinking 1 quart (0.95 liter) of alcohol daily for several years. Laboratory study revealed a blood picture characteristic of pernicious anemia with a hemoglobin level of 7.3 grams and an erythrocyte count of 2,500,000. Urinalysis demonstrated an occasional leucocyte and occasional granular and hyaline casts.

Pentothal and curare were selected for use. The mouth and pharynx were sprayed with cocaine, 10 per cent. In the 15 minutes preceding the suspension laryngoscopy, 60 units of intocostrin (*N. N. R.*) were given, followed after a 5 minute interval by 0.5 gram of pentothal in a 10 minute period. When the suspension laryngoscopy was begun, the patient objected to the procedure. During the next 15 minutes an additional 20 units of intocostrin and 0.6 gram of pentothal were given. During this period two brief episodes of laryngospasm occurred. The anesthesiologist was palpating the pulse at the wrist when the pulse suddenly disappeared. Respirations ceased also. The surgeon had a long biopsy forceps in his hand and was looking directly at the cords when this occurred. He immediately used the forceps to hold the cords open while artificial respiration was carried on. When this produced no results in about 3 minutes, a flexible metal endotracheal tube was inserted and artificial respiration was carried on by pressure on the breathing bag of an anesthetic machine, using the closed system. Nikethamide, 15 cubic centimeters, was given with no effect. Ten minutes after the cardiac arrest 1 cubic centimeter of epinephrine, 1 to 1,000, was infiltrated into the heart by means of a long needle. This dose was repeated in 5 and in 8 minutes. No effect could be noted. Artificial respiration was continued although livor mortis began to appear on the arms, legs, and back. Suddenly the pulse reappeared, approximately 25 to 30 minutes after it had disappeared. It was strong, with a rate of approximately 130 to 140 per minute. The livor mortis disappeared rapidly. In 10 minutes the pulse rate dropped to 60 per minute and remained there for about 5 minutes. The rate varied between 100 and 120 per minute from then on. Respiratory efforts did not reappear until 2 hours after the cardiac arrest and 1 hour and 30 minutes after the return of cardiac activity. In 3 hours, respirations were regular at 10 to 12 times per minute, but were of a gasping character. The patient did not regain consciousness. His temperature rose rapidly to a high level and he died 11 hours after the cardiac arrest. Permission for autopsy could not be obtained.

This case was thought to be significant for several reasons. It was believed that some cardiac activity must have been present at all times even though the pulse and blood pressure were not obtainable. Epinephrine was the only drug used to stimulate the heart and apparently was of some value. Finally, a cause for the whole episode could be found. Apparently, a wrong choice of anesthetic agent was made. Under pentothal anesthesia, the spleen may dilate and retain some of the circulating red blood

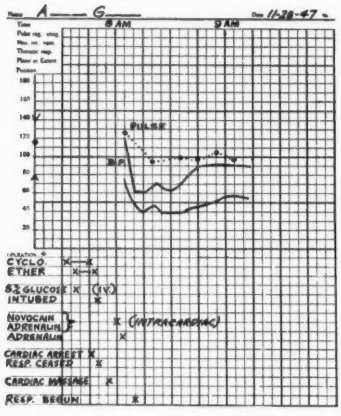

Fig. 7. Anesthesia chart. In this case cardiac arrest occurred early in the anesthesia period. The patient was given cardiac massage through an incision at the fourth left interspace. The surgeon introduced two fingers through the opening and massaged the heart against the chest wall.

cells within itself. Curare may also cause impaired venous return to the heart and a lowered cardiac output because of widespread muscle relaxation or a direct relaxing effect on the smooth muscle of the arterioles. The clinical cardiac arrest in this case could then be said to have a probable beginning in hypoxia of the cardiac musculature caused by the reduction in oxygen-carrying red blood cells brought about by the action of pentothal and curare which resulted in disturbed or inefficient cardiac action.

CASE 9. A man, aged 58 years, had withstood a pneumonectomy for carcinoma of the left lung with involvement of the pericardium, with no unusual difficulty, when cardiac arrest occurred as the subcutaneous layers of the chest wall were being closed. Artificial respiration was begun, the chest was immediately reopened, and the heart was found to be still. Cardiac massage was begun and feeble cardiac activity quickly returned. No pulse or blood pressure, however, could be detected by the anesthesiologist. With the heart under direct vision, the surgeon noted that its activity was becoming more feeble. A mixture of 0.25 cubic centimeter of epinephrine and 3 cubic centimeters of procaine hydrochloride, 1 per cent, was injected into the right ventricle. The heart beat became more forceful and soon after very rapid and irregular. In order to prevent fibrillation, 4 cubic centimeters of procaine hydrochloride, 1 per cent, were injected into the cavity of the left ventricle. Immediately following the injection of procaine there was noticeable slowing of the pulse. The blood pressure was then 120 millimeters systolic and 70 millimeters diastolic and the pulse rate was 120. The chest was closed without further incident. Convalescence was not unusual. The patient had a loss of memory of events beginning 24 hours before operation and was understandingly hazy on the first few postoperative days.

This case showed that cardiac activity can be present with no detectable pulse or blood pressure.

CASE 10. A woman, aged 26 years with Cushing's syndrome was scheduled for exploration of the adrenal glands. Cyclopropane was used for induction at 7:30 a.m.; ether was begun at 7:35 a.m., and cyclopropane was discontinued. At 7:48 a.m. cardiac arrest occurred. An endotracheal tube was immediately inserted and artificial respiration with 100 per cent oxygen begun. Procaine, 2 cubic centimeters of a 1 per cent solution, and epinephrine, 2 cubic centimeters, 1 to 1000, were injected into the heart with a long needle. The fifth interspace was quickly opened and cardiac massage carried out with two fingers against the heart. Injection of procaine and epinephrine directly into the ventricle was repeated. The cardiac beat quickly resumed and respirations soon followed. The blood pressure was 120 millimeters systolic and 70 millimeters diastolic and quickly fell to 55 systolic and 40 diastolic, then gradually rose to 90 millimeters systolic and 50 millimeters diastolic. The patient was returned to her room. She remained unconscious for 48 hours. At times she showed the picture of decerebrate rigidity with flexor spasm of both feet, spasticity of the right arm, and opisthotonos. Her eyes remained fixed with no reaction. Pulmonary edema occurred also. The patient gradually improved after 48 hours of unconsciousness. She appeared childish, then euphoric, then more mature. She was anesthetized again 8 days later with pentothal, curare, nitrous oxide, and oxygen. A bilateral resection of the adrenal glands was done uneventfully. This patient returned to her original mental state before operation (Fig. 7).

CASE 11. A woman, aged 22 years, came to the clinic because of congenital heart disease and a diagnosis of interauricular septal defect with poor cardiac reserve. On July 29, 1947, catheterization of the heart was carried out under local anesthesia with no ill effect. On August 1, 1947, the patient was scheduled for operation. Induction was begun with pentothal, 2.5 per cent. The pharynx and larynx were cocainized and an endotracheal tube was passed 12 minutes after induction was begun. Ether was begun with carbon dioxide absorption and circle filter. The patient was being put in position for operation in the operating room when cardiac arrest suddenly occurred. Thoracotomy was immediately done and cardiac massage started. Artificial respiration with 100 per cent oxygen was carried on. Procaine, 4.5 cubic centimeters, and epinephrine, 0.5 cubic centimeter, were injected into the heart. Forty minutes after cardiac arrest 0.5 cubic centimeter of epinephrine was injected into the cardiac muscle and repeated every 20 minutes. The heart beat suddenly returned after 1 hour and 5 minutes; 10 cubic centimeters of procaine were injected into the ventricle. The pulse was 110 per minute and the blood pressure 90 millimeters systolic and 60

millimeters diastolic. Arrest again occurred after 15 minutes. Activity returned after 10 minutes for only a short period. It ceased and activity did not return again, although resuscitative measures were continued for another hour and 15 minutes.

Autopsy revealed congenital heart disease with interauricular septal defect, aortic stenosis, hypertrophy of the pulmonary artery, hypoplasia of the aorta, and cardiac hypertrophy. Microscopic sections revealed minimal pulmonary tuberculosis and focal granuloma in the myocardium thought to be tuberculous in origin. Cardiac arrest was called the immediate cause of death.

CASE 12. A woman, aged 63 years, with hyperthyroidism had had long preparation with Lugol's solution and thiouracil before operation. Induction with 0.4 gram of pentothal, 2.5 per cent, was begun and ether begun in 10 minutes. The patient was intubated within 20 minutes. She was placed in position, the area of operation prepared and a low neck incision was made. At this point, cardiac arrest occurred. Procaine, 4.5 cubic centimeters, with 0.5 cubic centimeter of epinephrine was immediately injected directly into the heart ventricle by means of a long needle, its presence in the ventricle first being demonstrated by freely withdrawing 100 cubic centimeters of blood from the ventricle. Artificial respiration with 100 per cent oxygen was begun. Preparation for opening the chest was begun when the heart beat suddenly returned to its former rate and continued. The patient was watched carefully for 20 minutes. Then subtotal thyroidectomy was performed. Convalescence was normal and recovery complete with no cerebral changes (Fig. 8).

CASE 13. A 7 year old boy with congenital polyposis of the colon came to the clinic for colectomy. Induction of anesthesia with pentothal was uneventful, as was maintenance with ether on carbon dioxide absorption and circle filter. Two doses, 1 hour apart of d-tubocurarine, 5 units, were given. Operation progressed uneventfully for 1 hour and 25 minutes, when cardiac arrest occurred. Intubabation was performed immediately and artificial respiration begun. Subdiaphragmatic cardiac massage was started and 9.5 cubic centimeters of procaine, 1 per cent, and 0.5 cubic centimeter of epinephrine were injected into the heart through the left parasternal region. Procaine, 2 cubic centimeters, was given intravenously. The heart began to beat again within 5 minutes of arrest. At first the beat was irregular, then rapidly became regular. The blood pressure was 100 millimeters systolic and 40 millimeters diastolic and the pulse 160. The operation was quickly terminated and the patient returned to his room. He died 10 hours later in spite of all resuscitative procedures.

Postmortem examination revealed cerebral edema and patchy atelectasis of both lungs, with mucus plugs in the bronchi. The microscopic sections were of interest and are quoted: "In the Sommer's sector of the hippocampal convolution most of the nerve cells have disappeared and the remaining ones are darkly stained and shrunken. Astrocytes are slightly increased in number and size. Microglial cells are in transitional form and also have multiplied. In other parts of the cerebral cortex lesser degrees of nerve cell damage are noted. In some places nearly all of the nerve cells in the cortical layers, two and three, are shrunken and pyknotic and in others all the nerve cells in all the layers are affected this way. In some convolutions the majority of nerve cells are intact. The glial cells appear to be normal. Blood vessels and meninges are not changed. Scattered nerve cells in the thalamus, subthalamus, nucleus of Luys, substantia nigra, hypoglossal and inferior olivary nuclei are shrunken and pyknotic. This change was also noted in many of the Purkinji cells. The diagnosis was anoxic encephalopathy. Comment: Most of the nerve cell changes are acute, probably consistent with the duration of life after the cardiac asystole. The complete loss of nerve cells in one part of the hippocampal convolution and the gliosis are almost surely old lesions, probably related to anemic anoxia sometime in the past." The immediate cause of death was cerebral anoxia.

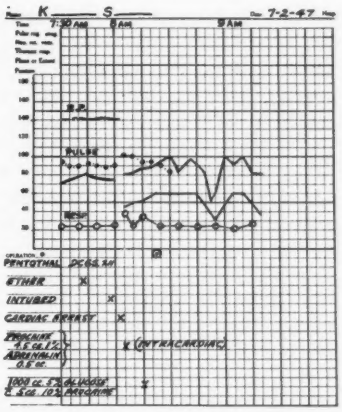

Fig. 8. Anesthesia chart. Cardiac arrest occurred shortly after the patient was intubated. The rapid administration of procaine and epinephrine brought about a quick return of cardiac activity.

COMMENT

Since this paper was completed, 2 more cases of cardiac arrest have occurred. The first was in an obese 72 year old man in poor general condition, who had a large retroperitoneal mass. Spinal anesthesia was given with 0.012 gram of pontocaine and dextrose, light supplementary anesthesia was induced with pentothal and anesthesia maintained with cyclopropane. Sterile drapes were being adjusted when the pulse and blood pressure suddenly

disappeared and the patient became cyanotic. An endotracheal tube was passed and artificial respiration with oxygen was begun. The surgeon quickly made an incision as planned for the operation, through the sixth left interspace. The heart could be seen beating regularly above the diaphragm. At this time the pulse and blood pressure suddenly reappeared and the cyanosis disappeared. The operation was continued. A large carcinoma of the stomach with retroperitoneal extension was found and a biopsy specimen obtained. The patient recovered from the apparent cardiac arrest, but died 2 weeks later from his advanced cancer.

The second episode occurred in a 67 year old physician who had successfully undergone subtotal gastrectomy and cholecystectomy under pontocaine-dextrose continuous spinal anesthesia and pentothal, 2 per cent, supplementary anesthesia. The surgical dressings had been applied. The trachea was being aspirated with a suction catheter when the pulse suddenly disappeared and the patient quickly became a mottled cyanotic color. An already prepared sterile set containing syringe, needles, and solutions was opened and 1 cubic centimeter of epinephrine, 1 to 1,000, and 3 cubic centimeters of procaine, 1 per cent, were injected through the fourth left interspace into the heart. The needle was left in place for a few seconds. It stayed perfectly still and then began to move as the heart suddenly took up its regular rhythm. The heart rate was 60 per minute at first and then increased to 120 per minute. This patient in his first few postoperative days showed no unusual effect from the cardiac arrest.

We still average 2 cases of cardiac arrest each year. The total now is 15. All hearts have been revived. Seven patients survived the complication and 1 patient appeared to recover but died on the second postoperative day of a coronary occlusion. Our survival rate at the present time is 46 per cent.

CONCLUSIONS

Cardiac arrest is an uncommon complication of a surgical operation. It is, however, a recognizable one, but requires acute awareness at all times by surgeon and anesthetist.

The heart can be started again in practically all cases that are true cardiac arrests, but probably 3½ minutes is the time limit available to restore heart action, and restorations beyond that time limit leave patients with irreparable cerebral damage.

Only organized teamwork, planned procedures, and readily available instruments and drugs make it possible to accomplish what must be done in 3½ minutes to retain the patient's mentality.

These cases will continue to occur. We must look on every patient who does have cardiac arrest as one which can literally and dramatically have his or her life saved if we can drill and train our operating room staffs and ourselves to do it.

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EDITORIAL

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EQUALIZATION OF LEG LENGTHS

DISCREPANCY in leg lengths is a common surgical problem, arising either from shortening or overgrowth. The most common cause of significant shortening results from anterior poliomyelitis in the growing child, but it may occur from congenital anomaly, epiphyseal injury, and various other causes. Discrepancy from overgrowth of an extremity occurs in congenital hypertrophy. It may be associated with vascular abnormality in the growing child, including arteriovenous aneurysm and with inflammatory lesions adjacent to the epiphyses, either within the joint or at the metaphysis. It may occur in such diverse conditions in the child as neurofibromatosis and overgrowth following fracture of the shaft of a long bone, particularly the femur. A fair percentage of individuals, moreover, have some mild discrepancy in length without evident cause.

If the inequality in length is small and amounts to no more than one-half to three-quarters of an inch, it usually is of little consequence, although such shortness produces a disturbance in the mechanics of the spine and may be a factor in causing back pain in the adult and need to be balanced by a lift to the heel of the shoe. The greater the discrepancy the more important it is to make up the inequality, at least in part.

Unfortunately, a discrepancy of two to three inches in the adult is not uncommon. A raise to the heel and sole sufficient to produce a satisfactory balance in weight-bearing in such an individual is unsightly and awkward, and, of itself, is a physical and psychologic handicap. Furthermore, if the shortness occurs in an extremity which has weak musculature, the heavy, cumbersome shoe may be the deciding factor that keeps the individual from discarding a brace. Under certain circumstances, slight shortness in an extremity is desired, as in a patient who wears a long brace, with the brace locked in extension. A shortness of one-half to three-fourths of an inch allows the individual to swing the brace more effectively. In almost all other instances, equal length is ideal.

Approaches to this problem of inequality of length have occupied the attention of surgeons for years. In 1905, Codivilla described a successful lengthening of a femur. Abbott[1], in 1927, described a technique of lengthening the tibia and fibula, and this procedure attained a considerable vogue for some years following. It is not too difficult in most instances, to obtain two inches lengthening of the leg of an older child or young adult which exhibits a considerable degree of paralysis in the lower portion of the extremity. However, it is a

[1]ABBOTT, L. C. J. Bone Surg., 1927, 9: 128–151.

procedure of considerable magnitude, requiring a long convalescence, and has a possibility of disturbing complications, including nonunion. The operation has lost favor, and is performed only under special circumstances. Other things being equal, however, one would much prefer to operate upon an abnormal, short leg, than upon the normal leg.

The procedure in the adult which is commonly employed is that of shortening the femur on the long side. Various techniques have been reported, including a simple overlap with pin fixation, as reported by White[2], and a "step-cut" with some type of skeletal fixation. It is a much simpler procedure than lengthening, has the healing time of a fractured femur, and has less likelihood of complication than does leg-lengthening. The tissues adapt themselves quite satisfactorily to the shortening of the long bone, up to an amount of two inches or so. The shortening of a long bone has the disadvantage that it is a procedure of some magnitude in the long leg, which often is the normal leg, and if significant complication should occur it would be serious. However, in the adult, it is ordinarily the procedure of choice.

In the child, however, the possibility exists of modifying growth to correct inequality in length. The ideal procedure would be one which would accelerate the growth of the epiphyses on the shorter extremity to the desired degree. Unfortunately, no dependable method to accomplish this has been developed. Although Harris and McDonald[3] and others have reported the value of sympathectomy for this purpose, there seems to be no uniformity of opinion regarding the results which are attained. However, the approach to correction of the discrepancy by inhibiting the growth of the longer extremity has been much more productive. This has taken the course of a surgical attack upon the growth of specific epiphyses, although other methods such as the use of roentgen radiation have been considered. Roentgen radiation does inhibit growth but the evidence up to the present time would seem to contraindicate its use in the human.[4]

In 1933, Dallas Phemister[5] described a procedure for the operative arrestment of longitudinal growth of bone. This involved the insertion of a bone graft across the epiphyseal plate on its medial and lateral side, following a curettage of the plate. In practice, the grafting was accomplished by removing a rectangular block of bone, which extended well across the plate into the osseous portion of the epiphysis, and even farther into the shaft. The graft was then rotated 180 degrees along a sagittal plane so that the solid bone of the graft was placed into the epiphysis and across the plate. This procedure, or one of its modifications, properly performed, stops the growth of the epiphysis.

This, alone, does not solve the problem as a working procedure, since it has the potentiality, by producing too much shortening, of doing as much harm as good. It is essential, in order for the procedure to be practical, to be able to predict within reasonable limits how much loss in length will be accomplished by the arrest of any particular epiphysis at any given age. In predicting the effect of an arrest, it is necessary to estimate, first, the growth to be expected in the lower extremity from any particular age to maturity, and, second, to know what percentage is contributed by each epiphysis. Epiphyses of particular importance in this consideration are the lower femoral and upper tibial and fibular epiphyses.

[2]White, J. W. J. Bone Surg., 1935, 17: 597–602.
[3]Harris, R. I., and McDonald, J. L. J. Bone Surg., 1936, 18: 35–45.
[4]Reidy, J. A., Lingley, J. R., Gall, E. A., and Barr, J. S. J. Bone Surg., 1947, 45: 853–872.
[5]Phemister, D. B. J. Bone Surg., 1933, 15: 1–15.

Hatcher adapted the anthropometric tables of Baldwin for the prediction of growth in the extremity, and used the figures of Digby as representing the percentage of growth which is contributed by the individual epiphyses. Percentages arrived at by Digby were obtained from anatomical material based upon the position of the nutrient artery in the adult, but, in the main, they have been substantiated by more recent observation.

Other methods of prediction have been developed, including the relatively complicated computation method of Gill and Abbott[6] who added the very important consideration of relative skeletal maturity in their estimates. It is well appreciated that children of the same sex mature at varying ages. In some children, the epiphyses may be closed at an age when other children still would have three or more years of growth remaining.

More recently, Green and Anderson,[7] after a 6 year study of the growth of the extremities in a longitudinal series of normal children, and of children affected in one lower extremity by poliomyelitis, published a table representing a guide for estimating the amount of growth which would be inhibited by the arrest of either of the epiphyses about the knee at various ages in the two sexes. The authors, in developing this chart, performed measurements at regular intervals using a special type of roentgenographic technique which recorded increments of growth. They determined the percentage of growth from each particular epiphysis in a group of cases, using as a guide the transverse lines of so-called "arrested growth." They evaluated the relative skeletal maturity of the children, using at each observation roentgenograms of the wrist and hand, after the method of Todd. The skeletal age was employed, both in the formation of the chart and in its use in prediction, when the chronologic age varied consistently from the estimated skeletal age by six or more months. They checked the results obtained in their patients who had had epiphyseal arrest against the predicted effect as indicated by the chart and found that the method was highly satisfactory in their cases. They did suggest, however, that the table was a guide only, upon which a clinical interpretation must be superimposed. They emphasized, too, that it was a report which was based on studies in progress since further years were necessary to develop a completely longitudinal series of observations.

The method has the advantage in that it is simple to use and seems to be the most practical method available. The chart shows deviations from the average, which allow for an adjustment of prediction on the basis of various modifying factors, such as the height of the individual and the relative inhibition in growth of the shorter side. The main difficulties in prediction arise from the difficulty in interpreting skeletal age and from the shifting pattern of skeletal maturity which occurs in a certain percentage of patients.

With the use of such a prediction chart, epiphyseal arrest or epiphysiodesis, performed at the proper time to accomplish the desired amount of shortening, is a very satisfactory method of correcting discrepancy in length of the lower extremities of the child. It is a procedure of relatively minor magnitude, although it must be performed with technical exactness. It is to be remembered in planning the time of the procedure that undercorrection is ordinarily preferable to overcorrection. If the shortening is considerable, it is often desirable to perform an arrest on one of the growth areas adjacent to the knee, say the tibial and fibula epiphyses, and then observe its effects for an interval, completing the in-

[6] Gill, G. C., and Abbott, L. C. Arch. Surg., 1942, 45: 286–315.
[7] Green, Wm. T., and Anderson, M. J. Bone Surg., 1947, 29: 659–675.

hibition by performing a femoral arrest when it is indicated at a later date. The interval method minimizes the difficulties that arise from inaccuracy of prediction and a shifting skeletal maturation. If too much correction is imminent after arrest, it may be necessary on rare occasions to perform an arrest on the short side in order to prevent overcorrection. Furthermore, almost all authors report a variable incidence of deformities which are due to unequal action of the arrest on the two sides. Green and Anderson believe that these should not occur and arise from technical factors. If they do, they may require secondary surgery for their correction.

Blount and Clarke[8] in an attempt to surmount the difficulties in prediction, recently made a preliminary report of the use of staples introduced so as to straddle the epiphyseal plate. The objective is to inhibit growth by the desired amount, and then to remove the staples, with the idea that growth will resume. This procedure is an outgrowth of the use of the wire loop by Haas[9]. The authors stated that they do not know how long staples may be left "in situ with the assurance of growth after removal," but have arbitrarily limited the time to two years, and "have encountered no untoward epiphyseal closures." They further stated that the time of doing the stapling is not important; that it can be done at any time, although usually not before the age of eight years, and that, when the desired correction in length has been accomplished, the staples can be removed with the idea that subsequent growth will not be affected. They exhibited certain patients in which growth had resumed, after removal of the staples, but they reported only isolated cases. The authors apparently have had considerable technical difficulties in their preliminary experiences with the method, although they believe that these have been largely eradicated.

Certainly a great deal more observation will be necessary before the value of this method in correcting discrepancy can be estimated and, in particular, before it can be determined how dependably growth will resume after removal of the staples. One would hesitate to depend upon such resumption of growth in a young child in an instance where deforming shortening would arise if the stoppage of growth continued following removal of the staples. For the present, if stapling is to be used, it would seem desirable to use prediction charts in deciding the timing of the procedure, with the idea that if growth does not resume after the removal of the staples, bothersome consequences will not result. The method gives promise but it must still be considered experimental and be used with discretion.

One must conclude that great strides have been made in recent years in correcting discrepancies in length of the lower extremities. Modification of growth in the child is a desirable method in many instances, but this should not be attempted except by a surgeon who is familiar not only with the technical factors involved, but with the vagaries of growth itself. The problem of each patient, furthermore, must be carefully analyzed prior to the interference with growth and thoughtfully followed until growth is completed.

WILLIAM T. GREEN.

[8] BLOUNT, W. P., and CLARKE, G. R. J. Bone Surg., 1949, 31A: 464–477.
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THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE fifth volume in the series *British Surgical Practice*,[1] takes the reader from "Hodgkin's disease" through "lymphogranuloma inguinale." This volume also contains extraneous subject matter which can scarcely be considered strictly surgical in nature but which will be of practical importance on rare occasions to the busy practitioner. Topics such as immersion foot, ischemia, leprosy, lipoid metabolism, lupus vulgaris and so forth might have been omitted from the ordinary surgical volume.

There is a rather complete dissertation on Hodgkin's disease with a thorough differential diagnosis and an excellent review of the pathologic manifestations. The stress laid upon proper and thorough roentgen-ray treatment is very timely and the results seem well borne out by experience in this country. Comment is made about the revival of modified dissection of the neck in certain cases but it is mentioned in passing only, which seems fitting in view of the excellent results now obtained by roentgen therapy. Points in diagnosis that are well taken are (1) sternal puncture, which is proving of great value in all centers in identifying lesions which might be confused with Hodgkin's disease and (2) biopsy of lymph nodes. There can be complete accord with the author who states that the cervical nodes are by far the best samples of the disease process. The pathologist may be hard put to make a diagnosis from an inguinal node which is characteristically confusing because of the multiplicity of infections which may be represented there.

Sir James Learmonth is responsible for the excellent chapter on hypertension. This chapter is true to the tradition of this particular set of volumes in that it is entirely in outline form which adds to, rather than detracts from, the usefulness of his contribution. In addition to supplying the practitioner with all of the information he needs to decide whether the patient might be considered a candidate for surgical therapy, the author gives illustrations of a diagrammatic nature to show the problems and criteria of a good operation. It is gratifying to know that no great claims are made and that each postoperative patient is considered and his own result is tabulated only after months of observation.

The chapter on intestinal obstruction manages to cover all of the important details taught in modern clinics. The pathologic physiology is outlined briefly; the danger and pitfalls are stressed. There is very brief mention of the proper use of the various indwelling nasal tubes but the references are clear and proper warnings are sounded about the absolute and relative contraindications to the use of a nasal tube as the sole treatment. An element of some surprise is the rather casual discussion of jejunotransverse colostomy in cases of ileus resulting from peritonitis. This particular operation has not gained a foothold in the United States and one might well question the advisability of including it in such a casual fashion in view of the fact that the occasional surgeon might be led to produce more harm than benefit.

The comments on obstruction of the colon are rather brief but appear to cover the usual salient features. The chapter ends with a summary of the rare tumors of the small intestine and goes on to a complete discussion of most of the information now available on the ulcerative and hyperplastic diseases peculiar to the terminal part of the ileum and right portion of the colon. A separate chapter on intussusception is well taken. Its illustrations are excellent as is the outline of diagnosis and treatment.

The chapter on jaundice of necessity is kept general and repeats the well accepted features which should be clear in the minds of those physicians entrusted with the care of such patients. The chapter is merely an introduction to the method of approaching the problem of jaundice and the proper way of going about the differential diagnosis. Fortunately, many of the authorities in this field are quoted freely and, at the end of the chapter, there is an indication of a more complete index under other headings.

There is a very thorough section on diseases of joints. It stresses correct diagnosis and has well illustrated portions dealing with the many aids to correct diagnosis. Some of the more common joint lesions and infections are discussed and, although necessarily outline in style, there is more than adequate information presented in a rather pleasing fashion. Toward the end of this section, there is emphasis on rather complicated operations which the average practitioner would do well to leave to the experienced orthopedic surgeon. There are numerous plates with reproductions of roentgenograms, especially as regards tuberculosis. Splints and other supporting appliances come in for their proper share of attention.

There is a rather detailed discussion of diseases of the kidneys and ureters, perhaps the best part of this present volume. The work seems complete in most details and the reader is spared any superfluous

[1] BRITISH SURGICAL PRACTICE. Edited by Sir Ernest Rock Carling, F.R.C.S., F.R.C.P., and J. Paterson Ross, M.S., F.R.C.S. Vol. 5. London: Butterworth & Co., Ltd.; St. Louis: The C. V. Mosby Co., 1948.

verbiage and unnecessary reference digest. The more common operations are mentioned and indications and shortcomings are well pointed out. It was surprising to notice the amount of attention given to the operation for denervation of the kidneys. The indications for that operation are said to be renal pain of unknown origin, nonmechanical hydronephrosis or pain due to nephroptosis. There appears to be considerably more enthusiasm in the British Isles for the operation than there is in this country. It might be said that many of these patients will present borderline psychoneurotic problems anyway and the exact indication for the operation would be open to considerable argument. Nonetheless, the author appears to be an authority and he is firm in his convictions about the benefits which might be realized. Throughout the entire work on the kidney and ureter there is repeated emphasis on proper and thorough examination, with adequate illustrations of the proper use of the many aids the urologist now has at his disposal. There is some discussion of chemotherapy and antibiotics but this has been kept rather short, perhaps because the author realized that by the time the work appeared in its final form, there would be considerable change in the thinking.

There is a most useful chapter on the larynx. In a busy surgical practice in a large city, the surgeon may tend to forget diphtheria and its distressing sequelae. This chapter outlines the modern-day thinking very well and stresses the proper use of tube and suction as well as reminds all practitioners of the ever present threat which may require tracheotomy. Toward the end of this chapter, the work becomes perhaps more highly technical than the average reader might appreciate. The treatment of tumors and rare lesions in this region would certainly be far better if left in the hands of an accomplished specialist, but the illustrations are well put and the knowledge that is available to the reader at least serves to stress what might be accomplished under proper conditions. The chapter also points out the shortcomings of certain procedures.

The volume has a separate chapter devoted to law in relation to surgery. The American surgeon will notice differences in the two types of legal systems but the moral obligations are well outlined and a practical common sense approach would certainly afford considerable protection for any surgeon regardless of where his practice might happen to be.

The volume finishes with some miscellaneous topics which were mentioned at the beginning of this review as being scarcely primarily surgical but, on rare occasions, calling for at least surgical consultation and the application of certain surgical principles to treat or avoid conditions which might otherwise result in serious complications. E. S. JUDD, JR.

THE work *Tumors of Bone*[1] has become so well established as a classic in its field that there is little to be written over and above the comments on the two previous editions. This reviewer has made such constant use of his second edition, it seems only necessary to investigate the recently added material.

New chapters have been added on fibrous dysplasia of bone, osteoid osteoma, and tumors of the spine. Separate discussions on endocrine changes in bone and rare diseases of bone have been included. The section on chondroblastoma has been altered in order to exclude controversial remarks. Giant cell tumor of bone has been reorganized for the better. The outline of contents is much more adequate and satisfying. It is easier to pick a selected topic for perusal. New cases are available and old ones are reclassified. The photographs of roentgenograms are clear and delineate the lesions thoroughly. Gross and microscopic photographs of the specimens are adequate in quality and in quantity. Remarks on the means of diagnosis and on treatment are concise. Some differences of opinion may arise concerning the various lesions which are benefited by radiation, surgery or a combination of both.

It would be helpful to have a small chapter on aspiration biopsy and immediate frozen section diagnosis on surgically excised material. The authors must be complimented for emphasizing the factor of a co-operative diagnosis by the surgeon, the roentgenologist, and the pathologist. In like fashion, they stress the advisability of having several pathologists review the histologic slides on debatable cases. So many nontumorous lesions of bone are included for completeness that the title could almost be changed to "Diseases of Bone." The print is clear and the binding is compact. This latest edition should be included in the libraries of all who deal with bone lesions and it should be readily available in all university and hospital libraries. M. C. WHEELOCK.

THE monograph *El diagnostico del embarazo con batracios machos*[2] narrates the experiences of Galli Mainini in developing the test for pregnancy which bears his name. It discusses the history and experiences which led to the discovery and the validity of the test. The observation as described revealed that the test was not a casual finding but was the result of scientific reasoning and tedious work on the part of the investigator.

The fundamental physiologic principle is based on the fact that the injection of urine from a pregnant woman into a male toad, Bufo arenarum Hensel, provokes the appearance of spermatozoa in the toad. The spermatozoa are obtained from the toad's cloaca by a specially designed pipette and are confirmed by microscopic observation. The control testing, using the urine of nonpregnant women, gives negative results as seen microscopically.

The details in technique are enumerated and illustrated as well as the method used in housing the animals. This latter has been designed particularly for the reuse of the animals in subsequent testing

[1] TUMORS OF BONE. By Charles F. Geschickter, M.D., and Murray M. Copeland, M.D. 3d ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1949.

[2] EL DIAGNOSTICO DEL EMBARAZO CON BATRACIOS MACHOS. By Carlos Galli Mainini. Buenos Aires: A. Impaglione, 1948.

and eliminating error of false positives arising from a too recent testing of the animal. It consists of a multiple compartment box in series which permits the advancement of a toad up to stall No. 1 from which it is taken when given a test. After the test it is placed in the end stall from which it is advanced again as the demand is made for further use.

Comparative data with many other similar tests for pregnancy show the favorable accuracy and economy in the Galli Mainini method. The greater part of the monograph is devoted to a critical analysis of the results obtained before the author reported his work in the literature. The book is an elaboration of his reports found in the recent English literature. Those interested in the original investigative procedures of this pregnancy test will do well to read the author's original work. STEPHEN A. ZIEMAN.

THE brief monograph *Observations on the Pathology of Hydrocephalus*[1] should effectively clarify the atmosphere concerning the pathology, particularly the pathogenesis, of hydrocephalus. The author has pointed out that hydrocephalus is due to a single cause, that of obstruction. This obstruction can be due to several factors.

It may follow the condition commonly known as atresia of the aqueduct of Sylvius, though usually such aqueduct pathology in the newborn is due to a "forking" or otherwise irregular and malformed canal. Atresia may indeed follow inflammatory conditions so that false membranes anywhere along the spinal fluid pathways, particularly the aqueduct, will act as a dam. Periaqueductal gliosis also may cause such obstruction. Variations in the Arnold-Chiari malformation may or may not be accompanied by hydrocephalus, but if hydrocephalus is present, it is due to the obstruction caused by that congenital defect. The author does not feel that the term idiopathic is justified among the causes of hydrocephalus. Depending upon their location, tumors may produce sufficient obstruction to cause hydrocephalus in all or in a part of the intracranial cerebral spinal fluid pathways.

In her several case reports and additional wide experiences, the author has not found any patients whose obstructive lesion could not be verified. Obstruction in the absorptive mechanism, the subarachnoidal villi, can be regarded as an obstruction to the flow of cerebral spinal fluid, and, therefore, one of the causes of hydrocephalus. The book is well illustrated and the brief case reports illustrative of the points made in the text. JOHN MARTIN.

TO those physicians who are interested in proctology, the book *Anus, Rectum, Sigmoid Colon*[2] by Bacon requires no introduction. The first and second editions, printed in 1938 and 1941 respectively, are well known for their detailed presentation of the various conditions which affect the terminal portion of the colon. The third edition is even more comprehensive. It is profusely and beautifully illustrated, and the bibliography is painstakingly thorough. Bulkiness, which was a minor fault of the earlier editions, has been corrected by printing the new edition in two volumes. The volumes are intricately organized, beautifully printed, and very readable.

To review the text chapter by chapter is not possible because of the magnitude of subjects discussed. No condition is slighted because of its rarity or relative unimportance. All material has been brought up to date, the book entirely revised. New chapters which have been added deal with actinomycosis, diverticulitis, volvulus, kraurosis, methods to relieve intractable pain incident to inoperable cancer, and the use of alloy steel wire sutures. In the discussion of all subjects the author has not limited himself to the ideas and procedures which to him seem the most applicable but has presented all pertinent material. Occasionally, perhaps, too much time and space has been allotted to methods of known limited value, but one gains the impression that this was done so that this work will rank second to none as a reference textbook.

One has no hesitancy in recommending this work either for the student of proctology or for the well trained, full time proctologist. JOHN R. HILL.

THE first edition of Mr. Gabriel's book[3] was published in 1932 and the succeeding volumes have covered more and more comprehensively all the common proctologic lesions. In the fourth edition, which comes in a scarlet jacket, the chapter on carcinoma of the anal canal which appeared in the third edition, is replaced by new material concerning anal incontinence and malignant disease.

Gabriel's *Rectal Surgery* is actually a presentation of the opinions and practices of St. Marks Hospital in London. The venerable institution was founded 114 years ago as "The Infirmary for the Relief of the Poor Afflicted with Fistula and other Diseases of the Rectum." The surgeons to this institution have traditionally served it long and faithfully. Its founder, Salmon, fostered the infant charity for 24 years, Goodsall for 33, and Allingham, Edwards, Gordon-Watson, and Lockhart-Mummery were all on the active staff for more than 20 years. Gabriel was appointed to its staff in 1920 and now, after 29 years of active service in its wards, is the distinguished senior surgeon of the hospital. Associated with him are a fine group of British surgeons actively interested in proctologic investigation and contributing freely to medical literature. This book reflects not only Gabriel's long experience but the work of

[1] OBSERVATIONS ON THE PATHOLOGY OF HYDROCEPHALUS. Medical Research Council Special Report Series No. 265. By Dorothy S. Russell. London: His Majesty's Stationery Office, 1949.

[2] ANUS, RECTUM, SIGMOID COLON; DIAGNOSIS AND TREATMENT. By Harry Ellicott Bacon, B.S., M.D., F.A.C.S., F.A.P.S., F.I.C.S., F.R.S.M. Vols. 1, and 2, 3d ed. Philadelphia, London, Montreal: J. B. Lippincott Co., 1949.

[3] THE PRINCIPLES AND PRACTICE OF RECTAL SURGERY. By William B. Gabriel, M.S. Lond., F.R.C.S. Eng. 4th ed. Springfield, Ill.: Charles C Thomas, 1948.

Nurbury, Milligan, Naunton Morgan and Lloyd David, and the fine scientific background of this unique institution.

The volume is not, however, insular in its scope. Writers of the United States in particular are freely quoted although emphasis is placed as would be expected on the procedures found satisfactory in London. The chapter on anorectal anatomy, a subject not properly presented in anatomical texts, will be of unusual value in comprehending and teaching this complex subject because of its lucid presentation. Colon surgeons will be especially interested in the description of the one stage perineoabdominal resection of the rectum for cancer originated by Mr. Gabriel in 1932, which is excellently illustrated. He prefers this procedure not only because of his own original training in the Lockhart-Mummery perineal resection, but because he has found it adaptable to poor risk patients and to those with large tumors which can be mobilized and displaced into the abdomen with more ease than in the reverse direction.

As is traditional with British medical writing, the language is simple, the concepts are easily grasped by the reader and a note of sincerity is constantly evident.

CURTICE ROSSER.

THE book *Fundamental Considerations in Anesthesia*[1] had its origin in the author's teaching experiences in the Army, where he instructed medical officers assigned to anesthesia duty. As a result the material presented is concise, lucid, and well organized. Many of the subjects discussed are inadequately covered in most textbooks of anesthesiology.

The volume begins with a brief outline of the fundamental anatomy, physiology, and pharmacology of the autonomic nervous system with emphasis on its pharmacologic aspects.

Respiratory patterns during the normal course of general anesthesia are clearly discussed with excellent diagrams to correlate with the text material. There follows comments on the abnormalities of respiration during general anesthesia. Two disturbances especially are dealt with—apnea from mechanical stimulation and apnea of biochemical origin—which are either omitted or incompletely presented in the usual reference book. A chapter is included on respiratory disturbances commonly or uncommonly encountered by the anesthesiologist, with a thorough discussion of the anatomy, etiology, prophylaxis and therapy of laryngospasm.

Under circulatory disturbances, the author takes up shock, including the most widely accepted theory of its development and the treatment of this condition after it has developed. He emphasizes prevention of shock and treatment of impending shock with some remarks on anesthetic preferences when the danger of shock is imminent. The pathologic physiology and treatment of celiac plexus and carotid sinus reflexes are discussed in detail. A separate chapter is devoted to the circulatory disturbances occurring during spinal anesthesia, with effects of posture, hemorrhage, histamine and carbon dioxide. There is also a chapter on cardiac arrhythmias. Parasympathetic reactions, both vagal and others, are comprehensively handled.

Finally the author discusses respiratory movements and their control during general anesthesia. An excellent section is presented on controlled respiration with the technique, indications, and disadvantages. Induced apnea, positive pressure respiration, and compensated respiration are also discussed briefly.

This volume is a distinct and valuable addition to the anesthesia library. The material contained in it can aid anesthesiologists greatly in understanding, preventing, and treating circulatory and respiratory aberrations seen under all forms of anesthesia.

RAY GIBSON PARRISH.

AS the title implies, *Pathology and Surgery of Thyroid Disease*[2] is a presentation about the thyroid gland, dealing primarily with the surgical and pathologic phases of the subject. As such, it will prove of more general interest to the surgeon than to the clinician and general practitioner. It will be of more value from the surgical than from the diagnostic point of view.

This book is a splendid work that should be read by all who are interested in thyroid disease. It is clearly written and informative, even including the most recent developments in radioactive iodine and the antithyroid drugs. In the first chapter the authors present a preview of the book that gives the reader a general summary of the subject. The chapters on anatomy, embryology, and physiology are well done. There is an excellent review of the work on blood iodine, and the authors cite their own studies in relation to the liver; they believe that blood iodine determinations seem to be an index of liver function, as well as of thyroid activity, rather than a mere measure of the latter. However, they conclude that blood iodine studies are not sufficiently accurate to be of important diagnostic value. Radioactive iodine and the antithyroid drugs are not considered to be of curative value in the treatment of toxic goiter, and at present thyroidectomy is still considered to be the most satisfactory method of dealing with toxic goiter.

Some surgeons will no doubt differ from this text on certain procedures Thus, hospitalization is advocated for at least 2 weeks prior to surgery in toxic cases, and bed rest is advised for 3 or more weeks for the more severe cases. Likewise, nitrous oxide is considered the anesthetic of choice, and superficial nerve block anesthesia is rejected because of inability of the patient to co-operate. Most surgeons now hospitalize these patients for only a few days, and, as Plummer pointed out, prolonged bed rest only increases the risk of operation.

[1] FUNDAMENTAL CONSIDERATIONS IN ANESTHESIA. By Charles L. Burstein, M.D. New York: The Macmillan Co., 1949.

[2] PATHOLOGY AND SURGERY OF THYROID DISEASE. By Joseph L. DeCourcy, M.D., and Cornelius B. DeCourcy, M.D. Springfield, Ill.: Charles C Thomas, 1949.

These criticisms are largely of minor significance, and we can highly recommend this book to anyone interested in this subject. ARNOLD S. JACKSON.

IN the recently published book, *Medicine Throughout Antiquity*,[1] the author cites facts that present some convincing evidence relative to man in his process of evolution and the diseases and injuries incident to his existence at intervals of time. The theory of evolution of man is well accepted at the present time; however, little is known as to the time element. The author in his discourse gives explicit data as to the methods of anthropologic and paleopathologic investigations and the interpretation of findings.

It would appear from the evidence presented that from the beginning man endeavored to sustain his life by procuring food, protecting himself against his enemies and relieving himself of the effects of injury and disease. This latter endeavor or urge seems to indicate an advancement from the purely instinctive action of animals to a thoughtful and planned solution of urgent problems. Therefore medicine, early in a crude form, has existed as long as man. There is evidence that 20,000 years ago the Cro-Magnons made special efforts to care for their injured and sick. In neolithic caves in France and Spain (7,000 B.C.) are drawings depicting amputations of legs and arms.

Incident to the study of fossils a fairly accurate account can be obtained about diseases that occurred in the far distant past, as well as some idea of the therapeutic procedures. Much information has been obtained by studying Egyptian mummies. As the author states, much credit must be given to Sir Marc Armand Ruffer for his intelligent and painstaking studies. He "deserves the credit for discovering a technique by which the desiccated tissues of the mummies, dead for 3 or 4 milleniums, are restored to a condition sufficiently soft to be examined under the microscope and thus detect pathologic changes which have taken place in their bodies during life." Further Ruffer found evidence of arthritis deformans from predynastic times to the third century A.D., a period of at least 8,000 years. He records a case in a Miocene period skeleton going back 900,000 years.

It is interesting to note that today there are many expressions that date back to antiquity. We speak of a "sad heart" or a "joyous heart." This dates back to the ancient Hebrews who considered such sensations as joy, fear, sorrow and pride as emanating from the heart and not the brain as we do today.

The author describes three periods of ancient medicine: the first, or prehistoric, a long period which began with the birth of man and ended when history began to be recorded; the second, or protohistoric, which began when history was first recorded and persisted until the beginning of the philosophical school of Ionia (600 B.C.); the third period began with the era of Ionian philosophy and ended with the fall of Rome. Information has been gleaned concerning the first period from studies of human fossils, crude carvings and paintings in caves and from stone instruments. Much interesting information is given about medicine in Assyro-Babylonia and ancient Egypt, of ancient Hebrew medicine, medicine in ancient Persia, India, China, Japan, and among prehistoric Amerinds. It is interesting to note that the Chinese have used a plant, ephedra, for more than 5,000 years in the treatment of hay fever. Our alkaloid, ephedrine, is obtained from this plant. The Chinese claim also to be the first to have vaccinated against smallpox. They inserted a cotton pad saturated with the contents of a fresh pox pustule into the nostril. In India as early as 550 A.D. the fluid from the pock from the udder of a cow was inoculated through a cut made in the back by a lance to prevent smallpox.

Some 300 pages are devoted to the Greco-Roman period. Since medicine was so closely associated with philosophy during this period, the student of history may be familiar with many aspects of this era. The medical profession is familiar with Aesculapius and Hippocrates and the great school of Greek philosophers. One cannot but marvel at the great intelligence of Hippocrates. With his age were associated the philosophers Anaximander, Heraclitus, Anaxagoras, Pericles, Alcmeon, Empedocles, Pythagoras, Diogenes and others. His immediate contemporaries were Herodotus and Thucydides, the two greatest historians of all times, Aeschylus, Sophocles, and Euripides, the great writers of tragedy, Aristophanes and Phidias, the sculptors. This was truly a galaxy of great men. Probably no man of medicine of any age has given so much to the medical profession as Hippocrates. It has been said that many of his clinical descriptions of diseases could be inserted in present day textbooks with but little if any alteration. In this section is included an interesting description of the Alexanderian School as well as of the Roman School, which includes Celsus and Galen.

This book gives not only an interesting and well authenticated description of medicine throughout antiquity but some record as well of the development of man from the earliest days, possibly hundreds of thousands of years ago. It should be of interest not only to the physician but to anyone who would follow man's climb up the ladder of development and civilization. It contains a stupendous amount of material which is magnificently presented and well illustrated. The author should be praised for the time and energy expended in gathering this mass of material and presenting it in such a readable form.

JOHN A. WOLFER.

THE *Textbook of Histology*[2] was developed by Drs. Nonidez and Windle according to the comments made in the preface. All statements are "concise"

[1] MEDICINE THROUGHOUT ANTIQUITY. By Benjamin Lee Gordon, M.D. Foreword by Dr. Max Neuburger. Philadelphia: F. A. Davis Co., 1949.

[2] TEXTBOOK OF HISTOLOGY. By Jose F. Nonidez, D.Sc., and William F. Windle, Ph.D., Sc.D. New York, Toronto, and London: McGraw-Hill Book Co., Inc., 1949.

and clear. "Controversial subjects" have been minimized. The explanatory format has assumed "little knowledge of anatomy and physiology" by the student for whom the volume is prepared.

It is easy to write an enthusiastic review of this book. The reasons will be obvious as they are enumerated. The arrangement attempts no dramatic change from the customary teaching methods. There is an analysis of the cell as a unit and the basic tissues are covered completely. The organs are presented *in toto*. Illustrations in the form of drawings and photomicrographs are in black and white and are properly selected and of the correct magnification. Emphasis is laid upon architecture rather than upon minute detail. This should enable the reader to attain the necessary facts as a foundation for the further study of physiology and pathology and ultimately the clinical sciences. The authors subscribe to the tenet that each subject in the medical curriculum is not a separate unit but rather that it should be blended with the other fields to turn out the finished graduate who will practice medicine rather than do research work. Knowing the limitation of time, the references at the end of each chapter number only 1 to 3, and these are selected with care. By use of dark type, attention is called to the cell, the tissue, or the structure under discussion.

Paragraphing is used frequently and the type is large and clear. Reading should be effortless. Reference to the page, while studying microscopic slides, should cause little confusion during the constant shift of vision.

This is an ideal text for the student. This reviewer predicts early acceptance by many universities. It should serve one further purpose. Today when many specialty boards require review of the basic sciences in preparation for certification, such a volume will aid materially in a quick review of histology.

It is a distinct pleasure to recommend this text.

M. C. WHEELOCK.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

THE 1949 YEAR BOOK OF RADIOLOGY (June, 1948–June, 1949). Radiologic Diagnosis edited by Fred Jenner Hodges, M.D., and John Floyd Holt, M.D. Radiation Therapy edited by Isadore Lampe, M.D. Chicago: The Year Book Publishers, Inc., 1949.

DIGITALIS AND OTHER CARDIOTONIC DRUGS. By Eli Rodin Movitt, M.D. 2d rev. enl. ed. New York: Oxford University Press, 1949.

MODERN PRACTICE IN ANAESTHESIA 1949. Edited by Frankis T. Evans, M.B., B.S., F.F.A.R.C.S., D.A. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1949.

MODERN PRACTICE IN OPHTHALMOLOGY 1949. Edited by H. B. Stallard, M.B.E., M.A., M.D., F.R.C.S. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1949.

THE DEVELOPMENT OF GYNAECOLOGICAL SURGERY AND INSTRUMENTS; A COMPREHENSIVE REVIEW OF THE EVOLUTION OF SURGERY AND SURGICAL INSTRUMENTS FOR THE TREATMENT OF FEMALE DISEASES FROM THE HIPPOCRATIC AGE TO THE ANTISEPTIC PERIOD. By James V. Ricci, M.D. Philadelphia, Toronto: The Blakiston Co., 1949.

CYSTOSCOPY AND UROGRAPHY. By J. B. Macalpine, D.Sc. (Honoris Causa), F.R.C.S.(Eng.). 3d rev. enl. ed. Baltimore: The Williams & Wilkins Co., 1949.

AN ATLAS OF AMPUTATIONS. By Donald B. Slocum, M.D., M.S. St. Louis: The C. V. Mosby Co., 1949.

DIAGNOSIS AND TREATMENT OF BRAIN TUMORS AND CARE OF THE NEUROSURGICAL PATIENT. By Ernest Sachs, A.B., M.D. 2d ed. St. Louis: The C. V. Mosby Co., 1949.

PHYSIOLOGY OF THE UTERUS. By S. R. M. Reynolds, M.A., Ph.D. 2d rev. enl. ed. New York: Paul B. Hoeber, Inc., 1949.

ANNUAL REPORT ON THE RESULTS OF RADIOTHERAPY IN CANCER OF THE UTERINE CERVIX. STATEMENTS OF RESULTS OBTAINED IN 1941 AND PREVIOUS YEARS (collated in 1948). Sponsored by the British Empire Cancer Campaign, London, The Donner Foundation, Philadelphia, The Cancerföreningen, Stockholm, The World Health Organization. Editorial Committee: Dr. J. Heyman, Editor, Stockholm, Dr. M. Donaldson, London, and Dr. L. C. Scheffey, Philadelphia. Stockholm: Kungl. Boktryckeriet. P. A. Norstedt & Soner, 1949.

ACUTE APPENDICITIS AND ITS COMPLICATIONS. By Frederick Fitzherbert Boyce, M.D. New York: Oxford University Press, 1949.

AN ATLAS OF THE BLOOD AND BONE MARROW. By R. Philip Custer, M.D. Philadelphia and London: W. B. Saunders Co., 1949.

THE EYE AND ITS DISEASES. By 92 International Authorities. Edited by Conrad Berens, M.D., F.A.C.S. 2d ed. Philadelphia and London: W. B. Saunders Co., 1949.

NORMAL VALUES IN CLINICAL MEDICINE. By F. William Sunderman, M.D., Ph.D., and Frederick Boerner, V.M.D. Philadelphia and London: W. B. Saunders Co., 1949.

DISEASES OF THE HEART. By Charles K. Friedberg, M.D. Philadelphia and London: W. B. Saunders Co., 1949.

THE SURGICAL TREATMENT OF FACIAL INJURIES. By Varaztad Hovhannes Kazanjian, M.D., D.M.D., and John Marquis Converse, M.D. Baltimore: The Williams & Wilkins Co., 1949.

HANDBOOK OF SURGICAL UROLOGY FOR INTERNES, HOSPITAL CORPSMEN AND NURSES. By Nelse F. Ockerblad, M.D., F.A.C.S. Baltimore: The Williams & Wilkins Co., 1949.

TRANSACTIONS OF THE SOUTHERN SURGICAL ASSOCIATION. Sixtieth Annual Meeting held at Greenbrier Hotel, White Sulphur Springs, W. Va., December 7, 8, 9, 1948. Edited by John C. Burch, Secretary of the Association. Vol. 60. Philadelphia, Montreal, London: J. B. Lippincott Co., 1949.